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RADIATION IN PRIMARY OPERABLE BREAST CANCER

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Until very recently, general acceptance of irradiation in breast cancer has been limited to postoperative therapy and to the palliative care of inoperable, recurrent and metastatic growths. The only contact with the disease in its more favorable stages has been that following operation. It is even questionable whether this has been as altruistic as might seem on the surface. All too frequently the case is referred, following operation, for postoperative irradiation as a gesture and for diplomatic reasons. Unfortunately, the manner in which the postoperative therapy, at times, is given, may justify to some degree this view on the part of the surgeon. In only a limited way has there been a close cooperation between surgery and radiation therapy in the field of breast cancer. While it represents one of the largest groups of cancer, it has not generally received the cooperative effort between surgery and irradiation that has been noted in certain other cancer groups. As far as the operable material has been concerned, radiation therapy—when employed at all—has for the most part been started after surgery has been finished.

It would seem that there is now sufficient reliable published information and an accumulation of experience to warrant a reappraisal of the situation. What position does radiation therapy now hold in the treatment of primary operable cancer of the breast? How may it be improved within those limitations? And how may its usefulness be extended? Do the surgical results warrant a complete right of way for operative measures in the technically operable cases? Has radiation therapy enough to offer to justify giving it precedence at any time in this group of cases? Does the accumulated experience with radiation in general warrant taking a bold step into the semidarkness for the benefit of such a desperate disease?

While no such clear-cut definition of controllability by irradiation has been made in breast cancer as with the epidermoid carcinomas, it is my opinion that the accumulated experience is sufficient to warrant advancing of the status of irradiation in the breast group. It deserves initial consideration in the entire primary operable group—not in a competitive but in a cooperative way. It has sufficient to offer to warrant delay in operation for thorough preoperative irradiation. There is neither need nor justification, except in certain special cases, for operation the morning after the making of a positive clinical diagnosis. Strictly operable tumors in elderly persons may well be a problem for radiation therapy rather than for surgery. The same may be true for the very young. Advanced growths, still considered operable by many surgeons, will probably do better by irradiation than by surgery.

There is a surprising uniformity in the surgical statistics from large clinics on the three and five year results of surgical treatment alone. The cases without axillary node involvement show a five-year curability of from 70 to 75 per cent. Harrington's [1] series was 71.2 per cent, and this may be considered a fair average. This seems, at first, most reassuring, yet Portmann reports that 95 per cent of all patients coming to operation have axillary nodes involved. The same author reported from the compilation of a large series of statistics that the average length of life in breast cancer, untreated, is thirty-four months, and that the average curability after operation, in the entire operable group, is 38.6 per cent for the three-year and 28.8 per cent for the five-year period. Sampson Handley [2] states that 70 per cent of all patients coming to operation have intrathoracic involvement. After a most exhaustive study of the records of patients operated on at Johns Hopkins from 1889 to 1931, Dean Lewis [3] concluded that, while the results for the first five years are encouraging, nearly all die of cancer ultimately. He distinguishes between "clinical" cancer and cancer in the "pathologic" sense and urges the most extensive operation possible on the ground of avoiding local recurrence and hence prolonging life in comfort for a longer period. He bases the only possibility of preventing local recurrence on this wide removal, especially of skin.

When the evidence is carefully gone over, the fact remains that of all patients coming to operation at least 70 per cent are dead from extension of the disease at the end of five years and that the majority of the remaining 30 per cent die of cancer ultimately.

With the known and proved value of the physical agents in cancer, and in the face of such a gloomy picture from surgery alone, it seems evident that radiation therapy should be pressed more aggressively in the so-called operable stages of breast cancer rather than limited to the follow-up phase of therapy.

Unfortunately, the relative radiosensitivity between different types of breast cancer is not as well understood or apt to be as clearly defined as in epidermoid

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1. Harrington, S. W.: Carcinoma of the Breast, Surg., Gynec. & Obst. **56**: 438 (Feb. 15 [No. 2A]) 1933.
2. Handley, W. S.: The Place of Radium in the Treatment of Breast Cancer, Practitioner **125**: 453 (Oct.) 1930; Treatment of Breast Cancer, Lancet **1**: 986 (May 7) 1927; Cancer of the Breast, ed. 2, New York, Paul B. Hoeber, Inc., 1922.
3. Lewis, Dean, and Reinhoff, W. F., Jr.: A Study of the Results of Operation for the Cure of Cancer of the Breast, Ann. Surg. **95**: 336 (March) 1932.

carcinomas, especially those of the mouth and cervix uteri. There are differences between these groups and beyond the histology of the tumor itself. The complex breast structure affords a peculiar tumor bed. The amount of fat tissue in both breast and axilla is of little value in supporting an otherwise normal reaction to irradiation. The mode of dissemination of breast cancer, along multiple paths and through both lymphatics and blood vessels, discounts to some degree the value of local histologic appraisals. The variations between tumor grading and relative radiosensitivity are greater in the breast group than in most of the other major cancer groups. In spite of this, continued study, correlating the microscopic changes with the clinical reaction to irradiation, will go far toward pointing out those groups most amenable to radiation therapy. At present the differentiation rests largely on an anatomic basis—the gross extent of the disease.

In an appraisal of radiation in operable breast cancer, it must be considered (*a*) in conjunction with surgery and (*b*) as the sole means of treatment.

SURGERY COMBINED WITH RADIATION THERAPY

From the standpoint of conjunction with surgery, irradiation may be employed as a preliminary to operation, as an adjuvant following operation, or as an accessory aid—castration and total body irradiation—and at the time of operation.

1. *Postoperative Irradiation.*—It is in this form that irradiation is most generally accepted and employed. Recognition of its value is unanimous among radiologists and is gradually gaining favor with surgeons otherwise disinterested in radiation. A number of recent and excellent reports by radiologists give statistical proof of the value of this form of therapy. Evans and Leucutia [4] have reported on the five-year results in a series of 173 cases. Surgery and postoperative irradiation gave freedom from clinical evidence of disease of 76.4 per cent for three years and 70.5 per cent for five years, in cases without axillary node involvement. Their comparative surgical results were practically identical, and from this they inferred that postoperative irradiation in this group was probably of no value. The inference is perfectly logical, since the disease was strictly local and the therapy followed operation. Further reference, however, will be made to this point under preoperative irradiation. In their cases with axillary node involvement the curability with surgery and postoperative irradiation was decidedly better over a five-year period than in their surgical group alone. Their group of semiradical operative cases followed by irradiation gave better five-year results than radical operation with no irradiation. This is very interesting, but it is to be hoped that it will not be misleading. It is my opinion that surgery resorted to for direct attack on the disease ought to be as extensive as possible. There are indications for local surgery but under other circumstances, to be discussed later.

Portmann's results with postoperative irradiation give a five-year curability of 43 per cent, a gain of more than 10 per cent over his large compilation of results from surgery alone. It is interesting to note that this improvement in results (10 per cent) is approximately the same as attributed to the improvement in surgical results following Halstead's report in 1894 of the radical operation, which has since been the pattern for practically all extensive breast surgery.

The extensive and complete report by Pfahler [5] on more than 1,000 cases in various stages gives the best figures for a combined group, 46.6 per cent of freedom from evidence of disease at the end of five years. He concludes that this is a gain of 90 per cent as compared with surgery alone. The uniformity of these results by independent clinicians is impressive and cannot fail to carry conviction.

There is danger, however, in statistics in the present phase of the development of radiation therapy as far as breast work is concerned. Surgery of the breast has been practically standardized since Halstead's notable publication in 1894, and supplemented by his improvement in adding removal of the pectoralis minor muscle a couple of years later. The procedure has been universally followed and the intervening period of nearly forty years has given excellent opportunity for the collection of most valuable statistics. The review of the entire Johns Hopkins work, including the original work of Halstead, by Dean Lewis is one of the most valuable. Never again will there be a period in which such data will become available from a surgical point of view alone. Irradiation is now complicating this phase of the picture. The period in which all the surgical data have been accumulating is longer than the entire lifetime of radiation therapy. Accurate scientific irradiation is a matter of only a few years and technical improvement is more active now than at any time in the past. It must be remembered that five-year results reported today are the result of work that has become technically obsolete in the interim. The persistent queries of the critics of radiation therapy are not sufficient urge to rush toward premature publication where the results are steadily improving under advancing methods. The careful conscientious observations from day to day and from year to year of the most experienced radiologists are infinitely more valuable. If the opinions of such men are not respected, neither will their statistics be respected. Surgical statistics are different. They are backed by time, uniformity of technical procedure and a large volume of material from many sources. As it is, comparable statistics will be difficult to find when the time is ripe for comparison. Too little attention has been given to grouping on the basis of the anatomic extent of the disease. Subdivision of the cases on a gross clinical basis after the plans of Schmitz [6] or Steinthal is essential if statistical data are to be of real value ultimately.

The practical need among radiologists today, as far as actual postoperative irradiation is concerned, is not a question of the advisability of it; that is accepted. It is on the uniformity of technical procedure, the time to begin it, the intensity and quality of the irradiation, and the areas to be covered. I believe that maximum efficiency, within the limitation of postoperative irradiation, demands beginning treatment as soon as initial healing has taken place. The shortest wavelengths have proved so far to be the most effective in cancer therapy, and there is no logical reason why the breast should be an exception. The superficial character of the local field and the possibility of serious intrathoracic damage are not logical contraindications. The accessibility of

4. Evans, W. A., and Leucutia, Traian: Deep Roentgen-Ray Therapy of Mammary Cancer, Am. J. Roentgenol. **24**: 673 (Dec.) 1930.

5. Pfahler, G. E.: Results in Radiation Therapy in 1,022 Private Cases of Cancer of Breast, Am. J. Roentgenol. **27**: 497 (April) 1932.

6. Schmitz, Henry: Five-Year End Results in Carcinoma of the Breast, Radiology **13**: 392 (Nov.) 1929.

the local field should be rather a stimulus to greater filter and higher voltages than an excuse for using a less efficient type of irradiation. Finzi [7] has stated it admirably by suggesting that postoperative irradiation should be quite as aggressive as would be the case were a recurrence actually present. The suggestion of Luff [8] that radium is preferable for postoperative therapy is undoubtedly due to the fact that the intensity of his radium therapy was much greater than his treatment with x-rays.

The same might well apply to Sampson Handley's preference for radium needles postoperatively, since he admits that he uses very low voltage roentgen therapy. After a radical operation the various and widespread areas that Handley most fears are more accessible to external therapy and better adapted to roentgen irradiation than to radium. Much has been said about intrathoracic damage, and it does occur in certain individuals; whether or not there is a variable sensitivity is questionable. However, many of the reported instances of such damage, if followed for a time, would prove to be extension of the disease. In dealing with a lethal disease, too much caution is more dangerous than an aggressive policy. The skepticism and uncertainty of many German radiologists on the subject of postoperative irradiation is undoubtedly due to inadequate dosage following an overindulgence in massive single doses during the early days of high voltage roentgen therapy.

No blanket rule can govern the areas of greatest intensity in the postoperative cycle. This should be dependent on the observations made by the surgeon at the time of operation and on the location of the primary tumor in the breast. The entire area to be irradiated, however, should be very wide. Dean Lewis has stated that the possibility of reducing local recurrence is dependent alone on the widest possible excision of skin. In my opinion and experience, wide and intensive roentgen irradiation will carry this needed insurance far beyond the borders of the most radical surgical sacrifice of skin, and very effectively. A very pertinent observation has been made by Harrington. He is not in favor of postoperative irradiation as a routine but advises it in cases of high malignancy. This is valuable in that it draws particular attention to the urgent need of extra help in such cases. If one may draw even a partial parallel with certain other tumors in the body, rated as highly malignant on a tumor-grading basis, it might even suggest the probability of accomplishing relatively more in this type, as far as the local and regional areas of possible involvement are concerned. The real danger, however, is from distant involvement, and it at once raises the question of the advisability of preoperative irradiation as an additional safeguard.

As to the time in which postoperative irradiation should be completed, individual operators have many and varied plans. It is the principle rather than minor details that is important. If one may draw on the experience of treating certain growths by irradiation alone, it would seem most logical to consummate the major portion of treatment within a period of from six weeks to three months at most. Sporadic and prolonged irradiation of low intensity is not in keeping with the most favorable general experience in radiation therapy.

2. *Preoperative Irradiation.*—I strongly believe that preoperative irradiation with x-rays of maximum intensity and quality offers more than any other phase of radiation therapy in primary operable breast cancer at the present stage of development of the use of irradiation in this disease. It has encountered much opposition. The majority of radiologists favor it but rarely have an opportunity to practice it. Just why some radiation therapists are opposed is difficult to understand. It is easier to understand why the surgeon opposes it. He is usually unfamiliar with irradiation on the one hand and is bound by the teachings of his preceptors on the other. From a study of the surgical statistics it is obvious that surgery alone has not enough to offer to warrant brushing aside a valuable aid for the sake of operating immediately. The only legitimate excuse for immediate operation is in the case of questionable clinical diagnosis in which frozen sections are necessary as a guide to the extent of operation. One requires only the experience of dealing with various phases of breast cancer by irradiation over a period of years to see the fallacy of Crile's [9] statement that, in the fortnight necessary for such treatment, cells not completely destroyed would be growing and extending. Total destruction of all cells is not expected; if such were the case, operation would be contraindicated. Many cells are completely destroyed. The chief effect, however, is inhibition, growth restraint, regressive and degenerative cellular influences on tumor bed as well as tumor cell. The most carefully done operation entails a substantial degree of trauma as a result of which tumor emboli are apt to be dislodged and carried outside the field of operation. A certain number of the 25 per cent of five-year fatalities following operation in the class 1 cases are undoubtedly due to dissemination at a distance at the time of operation. Postoperative irradiation does not get at these. They are outside the field of postoperative irradiation. Preoperative irradiation of adequate intensity is capable of reducing this type of dissemination. When axillary nodes are involved, it becomes even more valuable in this respect. One needs only to follow a series of these cases to appreciate the advantage of preliminary irradiation. Moran [10] has suggested that one of the theoretical justifications of preoperative irradiation rests on the classic experiments of Murphy of the Rockefeller Institute with irradiated tumor implants and implant beds. The skin will tolerate a minimum of 2,400 roentgens over a fortnight, with 200 kilovolts, a filter of 1 mm. of copper and 60 cm. distance, without serious interference with the surgical procedure. Preferably the operation should be deferred from six to eight weeks, until full effect of the treatment is manifest and most of the inflammatory effect has subsided. On account of the fibrosis, the axillary dissection is slightly more difficult; but healing is not impaired if rigid asepsis is maintained. In some instances, immediate operation following irradiation is called for. The patient's convenience or temperament may influence this. At that stage the operative field is more hyperemic, but healing will not be impaired if proper surgical technic is observed, although it is slightly delayed in rate.

Preoperative irradiation means roentgen irradiation. This type of treatment is not amenable to small surface

7. Finzi, N. S.: X-Rays and Radium in the Treatment of Carcinoma of the Breast, Brit. M. J. **2**:728 (Oct. 22) 1927.

8. Luff, A. P.: The Incidence of the Cancer of the Breast and Its History After Treatment, Brit. M. J. **1**:897 (May 14) 1932.

9. Crile, G. W.: Malignant Tumors of the Breast, with Special Reference to Management and End-Results, Bull. Am. Soc. Control of Cancer **14**, March, 1932.

10. Moran, H. M.: The Modern Treatment of Mammary Cancer, read at the Federal Cancer Conference, Canberra, March 27, 1931.

applications of radium, and radium by implantation is distinctly contraindicated. It is quite a different problem than treatment by radiation alone. The unfavorable comment abroad, especially in Germany, is due to small dosage and to zone irradiation that is too limited. In my experience, tangential irradiation is not practical. It is only in the occasional case that the method can be applied with any degree of satisfaction. Preoperative irradiation has been followed at Radiumhemmet for the past several years and Westermark,[11] reporting a small series, finds 40 per cent of all cases, classes 1, 2 and 3, free from evidence of disease at the end of five years. The figure is substantially better than similar groups of cases treated by surgery and preoperative radiation only (29.3 per cent). In my own material I have been impressed by the absence of skeletal metastases in the cases that have received preliminary irradiation of maximum intensity consistent with primary surgical healing. It may be a coincidence; a long period of observation alone will be conclusive.

All patients treated preoperatively should, following operation, receive postoperative treatment to the point of maximum skin tolerance. The only possible exceptions to this rule are the class 1 Steinthal cases. The point of concentration of this postsurgical irradiation should be dependent chiefly on the anatomic conditions found at operation.

Reports are occasionally made of inoperable breast cancer rendered operable by irradiation. In my judgment, breast cancer once inoperable is always nonsurgical as far as the direct treatment of the disease obtains. The more spectacular the regression, usually the more malignant, and hence the more dangerous from a surgical approach. It is at times very tempting to reconsider in favor of operation after a pronounced regression of a tumor primarily judged to be inoperable. The obvious benefit from the irradiation, however, had best be accepted gratefully and added to by the same agent. Indications for operation in such cases are usually not aimed at direct cure of the disease but for other reasons, and are usually local rather than radical procedures. The patient with a very large fat breast may well carry on more comfortably after a local mastectomy, or an area of impending secondary ulceration may to advantage be avoided by the same means.

3. *Accessory Irradiation.*—From time to time the question has been raised of possible added benefit through castration to the patient with breast cancer. Since it is so readily accomplished by irradiation of the ovaries, it is employed by some radiologists as a routine procedure when indicated. From a detailed study of the entire problem, Taylor [12] concluded that the ovarian hormone was a factor of influence. There seems to be no convincing evidence, however, of practical benefit through incorporating ovarian irradiation with preoperative and postoperative irradiation. In a small series of carefully observed cases at Radiumhemmet Ahlbom [13] was unable to find evidence that would support the theory in a practical manner.

4. *Irradiation at Time of Operation.*—In certain instances, radium by implantation, preferably radon in gold seeds, may be used to advantage, depending on the anatomic observations. Reference is made to the posterior portion of the axilla and to the upper intercostal spaces adjacent to the sternum, to which Sampson Handley has so frequently referred.

Before any extensive program of irradiation or surgery in operable breast cancer is assumed, a meticulously careful radiodiagnostic check up should be made of the chest and skeleton. It is a safeguard against grief and embarrassment in a few cases. The chief value lies in an early and permanent record for subsequent comparisons which symptoms may call for.

RADIATION AS THE SOLE MEANS OF TREATMENT

Experience is gradually accumulating on this vital and fascinating phase of mammary cancer therapy. Opinion will differ sharply as to whether the advising of such a procedure freely, in operable breast cancer, at the present time represents courage or foolhardiness. The conscience of the seasoned radiologist or cancer surgeon must be his guide. There may be a very nice distinction at this stage of the development of work between the responsibility one may assume under circumstances of strong personal pressure and the routine of professional work. At least there is a wealth of experience with all types of radiation and in all phases of the advanced disease as a background. There are a good many technically operable cases in which successful treatment over a period of years has been carried on. For one reason or another—age, general constitutional conditions or abnormal aversion to surgery—the radical operation has been withheld and irradiation substituted. On this basis alone, a substantial amount of material will be accumulated within a few years. To date, much of such material is of value only to those actually participating in the care of the individual case. Few biopsies have been obtained.

My first primary operable breast cancer treated by irradiation only, and now well over fourteen years ago, fails to be of value or conclusive to other than the three experienced cancer clinicians who concurred in the original clinical diagnosis, for just this reason: A woman, aged 49, had a tumor in the upper outer quadrant of the breast which was steadily progressing in size up to 2.5 to 3.5 cm. diameter, and over a known period of three months. There was a questionable node palpable low in the axilla. However, the case is best rated as Steinthal, class 1. For esthetic reasons—the patient was a concert singer—she was strongly opposed to surgery and knowing something of radiation pressed for treatment by the physical agents. She finally offered to assume her own future risk if I would but agree to this course. I treated her with the 1919 type of low voltage roentgen radiation and followed it by implantation of unfiltered radon into the tumor and the under surface of the free border of the pectoralis major muscle. The tumor regressed rapidly at first and then more slowly. After three years there was a dense residual mass in the breast and telangiectasis of the overlying skin, such as was common with that quality of roentgen radiation. There has been no noticeable change since.

Only a biopsy is necessary to make even one such case of that duration a matter of valuable record. Various authors, Moran and Wintz particularly, have pointed out that a biopsy is safe if deferred until a fortnight after irradiation has been initiated. By careful handling of tissues and through a small incision, placed as obscurely as possible, information may safely be obtained. The value as a future guide in therapy

11. Westermark, N.: Result of the Combined Surgical and Radiologic Treatment of Cancer Mammae at Radiumhemmet, 1921-1923, Acta radiol. **11**: 1, 1930.

12. Taylor, H. C., Jr.: The Etiology of Neoplasms of the Breast, Arch. Surg. **21**: 412 (Sept.); 597 (Oct.) 1930.

13. Ahlbom, Hugo: Castration by Roentgen Rays as an Auxiliary Treatment in the Radiotherapy of Cancer Mammae at Radiumhemmet, Acta radiol. **11**: 614, 1930.

adequately compensates the patient for the slight inconvenience, and it is invaluable to the future record. The theoretical objections to a biopsy are far outweighed by the practical information obtained. A tissue section represents the central point of the data-complex on which relative radiosensitivity is based, and on this in turn better radiation therapy is dependent. A biopsy by needle puncture under negative pressure is unsuitable for breast diagnosis except as a last resort.

Any attempt at this time to define the types of operable breast cancer which might justifiably be turned to irradiation entirely resolves itself into an expression of personal preference by the individual author. Certainly there should be little question about those suffering from a grave constitutional disease as well as the elderly and the very young. Elderly patients are prone to carry on for many years without treatment. In very young subjects, surgical results are so discouraging that any benefit from irradiation might well be considered a gain. Furthermore, the esthetic side in these patients lends strong support to the conservative method. In my opinion, cases with a long history of recognized tumor prior to seeking treatment should be considered poor surgical risks even though the local conditions place them in the operable class; irradiation instead might well be considered acceptable. This is equally true of cases of the advanced Steinthal class 2 group—those with extensive palpable node involvement.

One cannot help but admire the bold position taken by Geoffrey Keynes [14] and some of his associates in London. Since the London Cancer Conference of 1928, a number of English radiologists have become ultra-radium minded. It is questionable whether or not good judgment from a physical standpoint has kept pace with their bold stand on radium for breast cancer. At any rate, they seemingly stress the value of radium without giving quite as serious consideration to roentgen irradiation. It is a matter of individual opinion as to whether or not their recommendation of radium as the sole treatment for most operable breast cancers is premature. Keynes introduces radium needles, and for several days' exposure, on two occasions on each patient, each introduction being made under general anesthesia. Handley disagrees with the claimed uniformity of the distribution of radiant energy by his technic. Fitzwilliams [15] agrees with the Keynes technic and is seemingly more radical than the latter in his assignment of material to this method of treatment. Cade [16] endorses it but places added stress on surface applications of prolonged duration. The obvious factor of trauma incident to two introductions of many large radium needles, and each set must in turn be removed, is not in keeping with the generally accepted view of trauma in a tumor-bearing area. Mr. Souttar [17] has obviated this in large measure in his cases by using permanent gold-filtered radon implants. The two anesthesias give the impression of a major surgical procedure. In my own experience, external irradiation with x-rays, in intensity going far beyond that previously outlined for preoperative therapy, in multiple divided doses and of the shortest available wavelength, will afford complete local control of many breast tumors. A few cases extend now to six and seven years. In some instances the intensity requires implantation following the external irradiation, and for this radon in 0.3 mm. wall-thickness gold seeds is used. Radium for external irradiation, in quantities sufficient to parallel the present-day roentgen radiation, is neither economic nor practical.

Even though responsibility for the breast cancer in certain instances is placed on irradiation, a subsequent need for surgery occurs at times. In the very large pendulous fat breast, granting "sterilization" of the growth by irradiation, a simple mastectomy may render the patient much more comfortable. I cannot agree with Finzi that removal should be done as a routine after the tumor is "cured" by irradiation. There may well be justification for this position, however, in the scirrhous type of tumor, on account of its radioresistance and danger of subsequent reactivity. Secondary necrosis rarely occurs, but when it does, or preferably when it is threatened, local mastectomy is indicated for comfort and for the peace of mind of the patient. It is impossible to eliminate all surgery from any one group of cancers of the breast. Finally, while irradiation alone seems amply justified, in fact preferable, in certain groups of primary operable breast cancer, it also seems decidedly premature to regard it as the method of choice in the majority of cases. This is especially true in view of the marked improvement in results through combining preoperative and postoperative irradiation with the radical operation.

In attempting to make an appraisal of the probable value of irradiation in a given case, many factors must be considered. The histologic character of the growth is important and with added experience will become much more so. The size and location of the primary tumor in the breast, its known duration, presence or absence of axillary nodes, its location and extent are all important in selecting and directing the local irradiation. The age of the patient and the rate of growth are of value in governing the intensity of treatment. The general physical condition of the patient and the presence or absence of secondary anemia have substantial bearing on the probable manner in which irradiation will be tolerated and on the reaction to it.

Whatever agent, method or combination of x-rays and radium, with or without surgery, is decided on, no fixed routine plan is desirable. Adherence to fixed principles of therapy, rather than to fixed technical details, is the important factor. The factors of influence just previously mentioned must be correlated with what is expected to be accomplished by the irradiation.

THE RELATIVE VALUE OF X-RAYS AND RADIUM

In early breast cancer there seems little room for doubt that roentgen radiation occupies the major position. Most of the treatment is by external application and over wide areas; for this, x-rays are technically best adapted and most economic. Radium occupies a limited but valuable place, and always for implantation. Occasionally a primary tumor assigned wholly to irradiation requires implantation, and at operation radium by implantation may frequently be used to advantage in the axilla or the upper intercostal spaces adjacent to the sternum. For these purposes, radon in gold seeds affords a wide range or flexibility in application and is much less damaging from the standpoint of

14. Keynes, Geoffrey: The Treatment of Primary Carcinoma of the Breast with Radium, Acta radiol. **10**: 393, 1929; Treatment of Primary Carcinoma of the Breast with Radium, Practitioner **125**: 462 (Oct.) 1930; Radium Treatment of Carcinoma of the Breast, Lancet **1**: 439 (March) 1930.
15. Fitzwilliams, D. C. L.: The Modern Treatment of Carcinoma of the Breast, Practitioner **125**: 483 (Oct.) 1930.
16. Cade, Stanford: Cancer of the Breast, Practitioner **125**: 469 (Oct.) 1930.
17. Souttar, H. S.: Treatment of Carcinoma of the Breast by Radium Emanation, Brit. M. J. **1**: 813 (May 13) 1933.

trauma. Radium or radon implantation should always follow rather than precede the roentgen irradiation. Whatever the combination, and with few exceptions, the intensity of irradiation should be the maximum consistent with the tolerance of normal tissues within the zone of irradiation, and the quality always of the shortest wavelength available from up-to-date equipment. There is a limited time interval within which both the tumor and the tumor bed react most favorably to any type of irradiation, and improvement in results demands that advantage be taken of this. Meticulous attention to detail is quite as essential to success in radiation therapy as in surgery. As Moran has so aptly stated, "the careless radio-therapist, like the rough-handed surgeon, may cause grave mischief."

SUMMARY

1. Heretofore, irradiation has been limited almost entirely to postoperative treatment. Reference is made to primary operable breast cancer exclusively.

2. Postoperative irradiation has improved the five-year curability results.

3. The experience to date warrants advancing the status of radiation therapy in this group of cancer.

4. Preoperative irradiation is probably of greater relative value than postoperative.

5. In all cases of radical mastectomy, preoperative and postoperative irradiation should be employed.

6. While the ovarian hormone evidently exerts an influence on the development of some breast cancers, there is no substantial evidence to warrant castration by irradiation as a therapeutic aid.

7. As the sole means of treatment, irradiation is justifiable and undoubtedly preferable in certain cases.

8. To consider irradiation alone the method of choice in all cases of this group is premature.

9. Cases treated by radiation alone require biopsy not only for guidance in therapy but also to complete the record.

10. Biopsy is safe if carefully done after preliminary irradiation.

11. Of various methods of irradiation, preference has been given to x-rays for external therapy over wide areas and to gold seeds of radon for implantation.

12. X-rays occupy by far the major position in the radiation therapy of this group.

13. The same degree of attention should be given to technical detail in radiation therapy as in surgery.

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ABSTRACT OF DISCUSSION

DR. FRED O'BRIEN, Boston: The report on irradiation of breast cancer, which appeared in 1930 under the auspices of the American College of Surgeons, practically put an end to radiation therapy of the breast in my particular hospital for about two years because it was carelessly read and carelessly interpreted. Although Greenough stated that he was reporting statistics based on procedures of the decade 1910 to 1920 and that the data on irradiation were insufficient to form a basis on which to draw conclusions, I agree with Dr. Quick that the Halstead operation should be the standard operation, but it is far from being accepted by surgeons in general. There has been criticism of radiation therapy in the past because of the variety of methods employed, yet roentgen therapy has been in flux from the very nature of the thing, while the operation of Halstead has been known since 1894. There appeared a review in THE JOURNAL of operative procedures on the breast as practiced throughout the United States. It was found that only about 50 per cent of the surgeons employed the complete operation. It was most injudicious to be dogmatic about postoperative irradiation under those circumstances. I think that better results may be expected from clinics in which the surgical and the roentgen therapy methods are uniform. I think that Dr. Quick is correct when he says that it does not make any difference whether the patient is operated on the next day after the tumor mass has been found or two weeks from that time. These cases should be handled through a tumor clinic, so that patients will not get into the hospital before they have had their preoperative irradiation. Dr. Quick spoke about the time for postoperative treatment and said something about waiting for healing. My own feeling is very definite that irradiation does not retard healing; in fact, I know that it helps in the healing of many wounds. I have always thought that preoperative irradiation was most logical. If it is good afterward it ought to be equally good, if not better, before. I have seen no skin damage in recent years. Lord Moynihan stated in New York a few years ago that surgery had had its chance and had accomplished nothing and that he believed that now irradiation should be given its chance.

DR. U. V. PORTMANN, Cleveland: Dr. Quick has asked me to speak about the percentage of axillary involvement in my report of several years ago, which was based on statistics given by pathologists. I think the figure of 95 per cent of axillary involvement is probably a little too high and that it should be about 85 per cent. In other words, about 15 per cent of cases do not present axillary node involvement. This paper is not given with the idea of eliminating the surgical treatment of cancer of the breast but with the idea of proper treatment according to indications. With Dr. Quick, I think that as radiologists we should insist on some classification based on clinical rather than microscopic observations. It is my experience that I can tell more about what the subsequent course will be from the clinical story than I can from what the pathologist tells me. When a scirrhous type of growth is present, an entirely different clinical problem is presented than when more rapidly growing tumors are concerned. A tumor of long duration cannot be affected much by radiation and operation is preferable. Perhaps Dr. Quick will agree with me that the less clinically malignant, the less radiosensitive the tumor will be. I certainly agree with Dr. Quick that a primarily inoperable case never becomes operable. This applies not only to breast carcinoma but also to malignant neoplasms in any other place in the body. As Dr. Quick has prophesied, more cases of cancer of the breast will be turned over to the radiologist. But it is unfortunate that only about 15 per cent of all these patients have no axillary nodes involved and these are ideal for irradiation. As the skin becomes infiltrated by the neoplasm, the surgeon has a difficult task and I suppose that no surgeon will say that he can remove all the axillary involvement in 50 per cent of his cases. It has been my experience that a great many of them do not excise widely enough. It is in the operable cases that irradiation should be most valuable. In a great many the tumor itself can easily be eliminated by interstitial irradiation, and external irradiation will often destroy the skin extension.

DR. DOUGLAS QUICK, New York: I want to stress the need among radiologists to group these cases on some practical basis. While various means have been suggested, I lean toward the clinical and anatomic basis, because it is simple and permits of drawing rather straight lines. The group 1 cases are those strictly primary breast tumors without palpable nodes. The second class includes those with palpable, technically operable, nodes, and the third class, those with fixation of the primary tumor or with distant involvement. A good deal of knowledge on the relative radiosensitivity of these tumors is being acquired but it is not comparable with existing knowledge of radiosensitivity in certain other groups. Consequently it cannot be leaned as heavily on as a guide at the present time, but I think that a point will be reached where, from a histologic standpoint, one can pick out more definitely the types best suited to irradiation. I should like to stress the encroachment, if one chooses to call it that, of the radiologist on the breast cancer field. It represents a cooperative and not a competitive effort in any sense.

GASTRIC ACIDITY IN THYROID DYSFUNCTION

S. ALLEN WILKINSON, JR., M.D.
BOSTON

It has been recognized for some time that hyperthyroidism causes changes in gastric acidity and that in some cases there is an absence of hydrochloric acid. Hardt [1] in 1916 called attention to the fact that thyroid feeding caused lowered gastric acidity in normal dogs. Barker [2] in 1918 mentioned hypochlorhydria, and King [3] in 1919 noted that achlorhydria and achylia occur in hyperthyroidism. Lockwood [4] in 1925 and Moll and Scott [5] in 1927 reported a high incidence of achlorhydria in exophthalmic goiter. Following this line of thought, Truesdell [6] in 1926 showed that a lowering of acidity could be produced regularly by feeding thyroid to dogs, and in some achlorhydria was produced.

On the other hand, Crile [7] and his co-workers have held that the same mechanism that produced hyperthyroidism could in some cases produce peptic ulcer. He has also stated that denervation of the suprarenals and a hemithyroidectomy frequently relieves recurrent peptic ulcer. If this theory is true, hyperthyroidism should raise, not lower, the gastric acidity. Lerman and Means [8] have shown, however, that there is a definite tendency to lowered gastric acidity in hyperthyroidism and that the proportion of achlorhydria is increased beyond the normal.

This study was undertaken to show the relationship between hyperthyroidism and gastric acidity and to determine to what extent the acid returned to its normal level after relief of the toxicity. Also, we wanted to see what effect a postoperative lowering of the basal metabolic rate below the normal level would have on gastric acid.

This study comprises the results of gastric analyses in 100 cases of hyperthyroidism, taken before operation. At the Lahey Clinic it is the practice to have all patients return three months after partial thyroidectomy for a check-up metabolism. Of the original 100 cases, we were able to get only about one half back for check-up gastric studies. This was due partly to the reluctance of some patients to have a second test, partly to inability to return, and partly to the fact that three months has not elapsed since some of the original tests were made. It was felt, however, that for purposes of averages, a comparable number of postoperative check-ups would give as much information. Consequently, determinations were made in 114 cases. In addition, there was a much smaller group of patients with spontaneous myxedema who had had no operative history. Determinations were made in as many of these as possible, but cases of true myxedema are rare. Hurxthal [9] has shown that, in order to be classified as true spontaneous myxedema, the patient should first present the clinical signs and symptoms of the disease, secondly he should have a low metabolism and lastly he should have an elevated blood cholesterol. Many patients have a low metabolism but they do not fulfil the other two criteria and are not benefited by thyroid medication.

The method of gastric analysis used in this series was the same in all cases. A test meal of 50 cc. of 7 per cent alcohol was given on a fasting stomach after all the residual stomach contents had first been aspirated. Five minutes later a subcutaneous injection of histamine acid phosphate was given. The dose used was 0.1 mg. of histamine for each 10 Kg. of body weight. Fractional samples of the gastric contents were taken at thirty, sixty and ninety minutes. While it is usually customary to aspirate at fifteen-minute intervals and for a two-hour period, a short preliminary series indicated that, for all practical purposes, this test was just as accurate and much simpler. In no case in this series was acid obtained at the one and one-half hour extraction when it had been absent in all the previous extractions. The averages in this series were obtained from the maximum free and total acid values obtained during the course of each test.

TABLE 1.—*Hyperthyroidism: Averages Before Operation*

Metabolism	Cases	Basal Metabolic Rate	Free Acid	Total Acid	Variations in Acidity: Free Acid	Variations in Acidity: Total Acid
Over +35 with acid	40	+52	34.7	46.8	3-80	6-92
Under +35 with acid	24	+39	42.7	54.5	6-76	12-92
Over +35 without acid	30	+52	0	14.8	0	4-30
Under +35 without acid	6	+28	0	13.0	0	10-20
Averages, all cases	100	+42.8	24.0	38.9		

There is considerable divergence of opinion as to what constitutes the normal level of acidity. For my purposes in this paper the normal level is irrelevant, as the figures quoted are on a comparative basis rather than a fixed standard. Vanzant and others [10] have reported a large series with the standard Ewald meal and a single one-hour extraction. Histamine was not used as a routine in their series. They give the average figure for free acid at 40 and the total acid at 57. Lerman, Pierce and Brogan,[11] using an alcohol test meal and histamine, report the normal free hydrochloric acid as 40.4 and the total acid as 50.1.

In table 1 are the averages of 100 cases of toxic goiter; of these, 91 cases were primary hyperthyroidism and 9 were adenomatous goiter with secondary hyperthyroidism. Thirty-six patients had achlorhydria. In the group with free acid are included about ten patients who had a very low acid (under 10). As the table indicates, a large proportion of those who had achlorhydria fell in the group who had a basal metabolic rate higher than + 35.

From the Department of Gastro-Enterology of the Lahey Clinic.
The New England Deaconess Hospital Pharmacy furnished the histamine used in this study.
Read before the Section on Gastro-Enterology and Proctology at the Eighty-Fourth Annual Session of the American Medical Association, Milwaukee, June 13, 1933.

1. Hardt, L. L. J.: The Secretion of Gastric Juice in Cases of Gastric and Duodenal Ulcers, Am. J. Physiol. **40**: 314-331 (April) 1916.
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3. King, J. H.: Gastro-Intestinal Disturbances in Metabolic Diseases and in Diseases of the Ductless Glands, M. Clin. North America **2**: 1655 (May) 1919.
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5. Moll, H., and Scott, R. A. M.: Gastric Secretion in Graves' Disease, Lancet **1**: 68 (Jan. 8) 1927.
6. Truesdell, C.: The Effect of Feeding Thyroid Extract on Gastric Secretion, Am. J. Physiol. **76**: 20-27 (March) 1926.
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10. Vanzant, F. R.; Alvarez, W. C.; Eusterman, G. B.; Dunn, H. L., and Berkson, Joseph: The Normal Range of Gastric Acidity from Youth to Old Age, Arch. Int. Med. **49**: 345-359 (March) 1932.
11. Lerman, J.; Pierce, F. D., and Brogan, A. J.: Acidity in Normal Individuals, J. Clin. Investigation **11**: 155-165 (Jan.) 1932.

Table 2 shows the averages three months or more after operation in 114 cases. In this group, twelve, or 10.5 per cent, showed no acid, while 102, or 89.5 per cent, showed free acid. The level of acidity has risen in the whole group as well as in the cases in which there was free acid. The average free acid was 46, as compared with 24 in the group before operation. The highest level of free acidity before operation was 42.7 in the group with a basal metabolic rate of less than + 35, whereas in this postoperative group with free acid the average is 51.2.

Table 3 shows the results after operation in twenty-five of the original thirty-six patients who had no acid before operation. These check-up tests were all made about three months after partial thyroidectomy. In this group only three still showed achlorhydria, while twenty-two had regained their acid.

In table 4 are those cases presenting low metabolic rates. There were only five cases of spontaneous myxedema. One of these patients had been taking thyroid for two years, and it is interesting that she had achlorhydria. Of the other four who had never had thyroid, the minimum free acid was 83 and the maximum was 98. One of these patients was later found to have a duodenal ulcer. In the postoperative hypothyroid group, none of whom had the clinical signs of myxedema, the average acidity is also very high. I realize that this series is too small to justify any general conclusions, but it shows an interesting trend.

TABLE 2.—*Hyperthyroidism: Averages After Operation*

	Cases	Free Acid	Total Acid	Variations in Acidity: Free Acid	Variations in Acidity: Total Acid
With acid	102	51.2	63.5	5-95	23-110
Without acid	12	0	13.9	0	10-22
All cases	114	46.9	58.1		

ACHLORHYDRIA

Our figures agree quite accurately with those of Lerman and Means * with respect to lowering of acidity in toxic goiter. Their series of fifty cases shows 38 per cent of achlorhydria as compared with the figure of 13 per cent according to the observations made by Lerman, Pierce and Brogan [11] in a series of 200 normal persons. The latter figure of 13 per cent is much higher than that quoted by Bockus, Bank and Willard,[12] which was 5.7 per cent; but these last investigators used a bread and water test meal with histamine instead of an alcohol test meal. We are in agreement with Lerman and Means, who state that the achlorhydria cannot be accounted for on the basis of a general lowering of acidity. The average level of acidity is about one-half the normal, while the incidence of achlorhydria is increased at least four times.

While it is true that the majority of the cases of achlorhydria fall in the high metabolism group above + 35, this does not, in itself, seem sufficient to account for the figures obtained, as in the same group there were forty cases that showed an average free acidity of 34.7. In searching for a better explanation, we investigated the duration of symptoms of toxicity and found that, whereas the group with free acid showed an average duration of 9.2 months and 68 per cent of this group an average duration of only 3.8 months, the achlorhydric group showed an average duration of 16.6 months, and only two cases in this group had had symptoms less than six months. It seems, therefore, that the development of achlorhydria depends on the duration rather than on the degree of toxicity.

Of more interest than the actual development of the achlorhydria is the fact that these patients recover their acid so promptly. Three months after relief of the toxicity, 89.5 per cent have recovered their normal gastric acid, and this recovery takes place as well in the anacid group as in the group with free acid. The rise of acid must take place fairly promptly, and apparently it returns to the normal level and even passes this level. We have no figures to show whether it later falls again.

TABLE 3.—*Results After Operation for Hyperthyroidism: Twenty-Five Cases with Achlorhydria Before Operation*

Original Metabolism	Cases	Free Acid Present*	Free Acid Absent
Over +35	20	18	2
Under +35	5	4	1
Totals	25	22	3

* Average free acid of this group was 44.

There have been theories as to whether the depression of gastric acid was a result of actual damage to the gastric mucosa or the result of some constitutional cause. Our observations do not indicate any damage to the gastric mucosa and point to a depression of glandular function. It is well recognized that most of the symptoms of hyperthyroidism are those of extreme overstimulation of the sympathetic system. It is also recognized that, when the sympathetic nervous system is stimulated, the autonomic system is correspondingly depressed. Might not this change in gastric acidity be an expression of the same mechanism that produces the warm skin, the perspiration, the tremor and general activation? Moll and Flint [13] have touched on this and point out that, both in man and in animals, epinephrine in sufficient doses over a considerable period of time will markedly depress gastric secretion and gastric acidity. They also point out that nicotine, which depresses sympathetic nerve endings, produces hyperchlorhydria.

TABLE 4.—*Low Metabolic Rates: Averages*

	Cases	Basal Metabolic Rate	Free Acid	Total Acid	Before Operation: Free	Before Operation: Total
True myxedema	5	−24	67.5	81		
Postoperative hypothyroidism	4	−23	81.9	94	22	37

MYXEDEMA

The evidence presented in the literature concerning gastric acidity in hypothyroidism is conflicting. Katz,[14] Levy [15] and Hutton [16] concur in stating that low thyroid function produces hyperchlorhydria. On the other

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13. Moll, H., and Flint, E. R.: The Depressive Influence of the Sympathetic Nerves on Gastric Acidity, Brit. J. Surg. **16**: 238-307 (Oct.) 1928.

14. Katz, J.: Deficient Thyroid Secretion as an Etiologic Factor in Gastric and Duodenal Ulcers and in Hyperacid Conditions, M. Rec. **97**: 916 (May 29) 1920.

15. Levy, M. D.: Endocrine Influence on Gastric Secretion with Special Reference to Hypothyroidism, New Orleans M. & S. J. **81**: 487-493 (Jan.) 1929.

16. Hutton, J. H.: Effects of Hypothyroidism, Illinois M. J. **42**: 337 (Nov.) 1922.

hand, Lockwood [4] found achlorhydria in 60 per cent of ten cases of myxedema. Lerman and Means [5] found nine cases of achlorhydria in seventeen cases of hypothyroidism. Our series is too small to be of much weight, but such evidence as we have points toward a definitely increased acidity in these cases. In those patients who conformed to the criteria for myxedema, the free acid was 67.5 and the total acid 81. In the postoperative low metabolism group the acidity was even higher. One of these patients had achlorhydria before operation.

SUMMARY

1. Of 100 cases of hyperthyroidism, 36 per cent showed achlorhydria, and the average acid of all cases was reduced to slightly more than half the normal.

2. The observation is made that the incidence of achlorhydria in hyperthyroidism rises in proportion to the duration of the toxicity rather than the degree of the toxicity.

3. After thyroidectomy, only 10.5 per cent show achlorhydria. The average free acid is raised to about the normal value for the entire series.

4. A theory is offered that the depression of gastric acidity is a phenomenon of extreme sympathetic overstimulation.

5. Hypothyroidism, in our series at least, produces a definite tendency to hyperacidity.

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ABSTRACT OF DISCUSSION

DR. RALPH C. BROWN, Chicago: The point of chief interest in Dr. Wilkinson's study is the evidence showing a return of normal physiologic activity in the gastric secretory glands after subsidence of hyperthyroidism following thyroidectomy. This evidence supplies what would seem to be convincing proof of the influence of thyrotoxicosis in suppressing gastric secretion. The fact that all but three of the twenty-five rechecked cases which had been achlorhydric under histamine prior to thyroidectomy regained an average free hydrochloric acid of 44 after recovery from thyrotoxicosis is of evident importance. This emphasizes the need for caution in assuming that a gastric secretory mechanism which fails to respond to histamine is likely to be permanently disabled. The presence or absence of the ferments is a much more reliable basis for a prognosis regarding possible future secretory activity. A review of seventy cases of hyperthyroidism and ten cases of myxedema treated at the Presbyterian Hospital in which gastric secretion studies were made, a standard Ewald meal without histamine being used, yielded figures somewhat at variance with those just reported. In nineteen cases of moderately severe and severe hyperthyroidism with basal metabolic rates ranging from plus 36 to plus 82, I found only three cases of achlorhydria, or 16 per cent, a figure only 3 per cent higher than the incidence of achlorhydria in otherwise normal individuals. There were five cases in the subacid group (free hydrochloric acid 1-20), nine cases presenting normal acid values (free hydrochloric acid 21-40), and two cases of hyperchlorhydria (free hydrochloric acid 41 plus). The average basal metabolic rate in this group of nineteen cases was plus 48. The average duration of symptoms of thyrotoxicosis was fourteen months. In the less severe group of thirteen cases, with rates ranging from plus 26 to plus 35, only one case of achlorhydria was found, six of these cases presenting a normal acidity and six definite hyperacidity. Combining these figures, one has thirty-two cases of hyperthyroidism, in which only four, or 13 per cent, presented achlorhydria. The average metabolic rate for the entire group was plus 41. The average acidity was 32 points of free hydrochloric acid, and the average duration of toxic symptoms was 16.8 months. It may be worth noting that in a larger series, thirty-nine cases, of mild but (according to my point of view) definite cases of hyperthyroidism showing rates ranging from plus 16 to plus 25, I found four achlorhydrias with only five subnormals; nineteen cases, or 50 per cent of the group, showed normal gastric secretion; and eleven cases, hyperchlorhydria. The average duration of symptoms was twenty months. Regarding hydrochloric acid values in myxedema: In ten cases in which the basal metabolic rates ranged from minus 22 to minus 47, and an average of minus 32.6, two were anacid, four were subacid, three gave normal hydrochloric acid values and only one showed a hyperacidity. Again, the number of cases is small, but the observations certainly do not suggest a tendency to hyperchlorhydria in myxedema. Lerman and Means found nine cases of achlorhydria in seventeen cases of myxedema. I should like to ask Dr. Wilkinson whether evidence of any marked lowering of pepsin and rennin secretion was observed in these cases during the achlorhydric phase; also whether any observations were made indicating any greater incidence of gastro-intestinal symptoms, especially diarrhea, in the achlorhydric group of cases than in the cases of acid secretion.

DR. S. ALLEN WILKINSON, JR., Boston: I am indebted to Dr. Brown for his discussion. I do not know how to explain the divergence in figures he has quoted as compared with mine. It is true that in my first twenty cases I failed to find any unusual incidence of achlorhydria. I have no idea why this happened. With regard to changes in gastric ferment, I did tests for gastric rennin in ten cases of this series who showed achlorhydria. Rennin was present in all of the ten cases, and there were none which I could call achylia gastrica.

METABOLIC ACTIONS OF DINITROPHENOL

WITH THE USE OF BALANCED AND UNBALANCED DIETS

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AND
M. L. TAINTER, M.D.
SAN FRANCISCO

Dinitrophenol (1-2-4) has been shown to increase promptly the metabolic rate in man and laboratory animals to almost any desired level. This action is peripheral, in the tissues, and independent of nervous and glandular functions. Small doses cause a slight increase in oxygen consumption; larger doses cause heat production that may surpass the ability of the animal to dissipate it, so that death occurs from heat rigor.[1] We [2] have suggested that, in proper dosage, dinitrophenol would be a potent therapeutic agent in obesity and in conditions in which a heightened metabolism might be desired. In a consideration of such possible uses the question arose of the source of the fuel for the increased metabolism. That is, dinitrophenol might promote the burning of carbohydrate, fat or protein, or all these fuels equally readily. A selective action on some one fuel appeared unlikely. An attempt was made, therefore, to study this question for human metabolism, experimental diets applicable to clinical conditions being used. The results are reported in this paper. Briefly, the results show that during medication with dinitrophenol the human body can maintain nor-

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2. Cutting, W. C.; Mehrtens, H. G., and Tainter, M. L.: Actions and Uses of Dinitrophenol, J. A. M. A. **101**:193 (July 15) 1933. Tainter, M. L.; Stockton, A. B., and Cutting, W. C.: Use of Dinitrophenol in Obesity and Related Conditions, J. A. M. A. **101**:1472 (Nov. 4) 1933.

mal nitrogen and acid-base balances while reacting with the usual increase in metabolism, regardless of the type of food consumed and without undesirable symptoms.

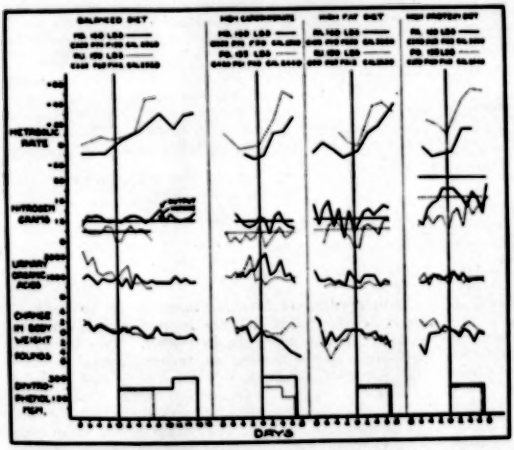
METHODS

Eight experiments were made on four subjects with four different diets, each diet being taken by two different individuals. In each experiment a subject was placed on a given diet for two weeks or longer, and his body weight, basal metabolism, nitrogen balance, and urinary organic acids were determined at regular intervals. The first week served as a control period without medication. Immediately following, during the second week, occurred the experimental period with dinitrophenol. The diets in all cases contained 40 calories per kilogram of body weight, a value considered to be adequate for subjects leading a sedentary life and possessing a normal metabolic rate. The diets were all carefully prepared and controlled in the special diet laboratory of the Stanford hospitals. Fluids were not limited. Each subject was weighed daily at the same hour. Nitrogen intake was calculated from protein intake, 6.25 Gm. of protein being used as the equivalent of 1 Gm. of nitrogen.

The metabolism was determined under basal conditions early in the morning, three times a week. No food or fluids were taken for at least twelve hours before the metabolic test, and there was a rest in bed of half an hour immediately preceding it. Twenty-four hour specimens of urine were collected daily and analyzed for urinary nitrogen by the macro-Kjeldahl method. To the value for urinary nitrogen output there was added an arbitrary value of 1.3 Gm. as an average value for daily nitrogen in the feces.[3] The values for nitrogen output throughout this paper are the sum of these two quantities. The organic acids in the urine were estimated by the titration method of van Slyke.[4] The values are expressed as cubic centimeters of tenth normal hydrochloric acid, required for the neutralization of the urine in twenty-four hours. It was assumed that, if the acid-base balance was disturbed or if acetone bodies were excreted, the organic acid figure would be increased. The dinitrophenol was administered in capsules as a single daily dose by mouth and before breakfast.

REGULAR DIET

In the first experiment, the subjects were placed on diets containing 1 Gm. of protein per kilogram of body weight, with the carbohydrate and fat apportioned about equally as to caloric value. This constituted an essentially normal balanced diet. For subject M. O., who weighed 74 Kg., the diet contained 2,960 calories and was made up of 308 Gm. of carbohydrate, 74 Gm. of protein and 150 Gm. of fat. The diet for subject R. U., who weighed 63 Kg., contained 2,520 calories and was made up of 263 Gm. of carbohydrate, 63 Gm. of protein and 142 Gm. of fat. After a week of control observations, the first subject was given 225 mg. of dinitrophenol daily for eleven days, followed by 300 mg. daily for five more days. The second subject was given 225 mg. daily for seven days. The results obtained are presented in the accompanying chart.



Effects of the administration of dinitrophenol on human subjects on balanced and unbalanced diets: composition of the diets for each subject, metabolic rate, total daily nitrogen intake and output, total daily urinary organic acids, changes in body weight and dosage of dinitrophenol.

The metabolism in M. O. rose from an average control of — 10 per cent to + 30 per cent, or a rise of 40 per cent, by the ninth day of medication with dinitrophenol and remained at this level for the next seven days. In R. U. the metabolism rose from a control of + 5 per cent to + 45 per cent, or a rise of 40 per cent, by the sixth day of medication with dinitrophenol and remained at this level for the next two days.

In M. O., the daily nitrogen intake was 11.8 Gm. and the output varied from 11 to 14 Gm., with an average of approximately 12.8 Gm. throughout both the control and the experimental period. The daily nitrogen intake for R. U. was 10.1 Gm., and the output varied from 8 to 11 Gm., with an average of 10 Gm. throughout both periods. Therefore the dinitrophenol produced no significant changes in nitrogen balance. The organic acids in the urine were constant at about 800 cc. throughout for M. O. and fell from an average of 1,500 to 750 cc. in R. U. during the action of dinitrophenol. Therefore there was no increase in acid bodies in the urine following administration of the drug.

M. O. lost 2 pounds (0.9 Kg.) during the control period and about 1 pound (0.45 Kg.) during the dinitrophenol period. R. U. lost weight similarly. With so short a period of medication with dinitrophenol as one week, the weight changes are not striking. A loss of weight might be expected unless the caloric intake was adequate to provide for the increased metabolism. This would not have been the case if the control diets had been just adequate for maintenance at normal metabolic levels, as planned. However, since the water intake and the activity of the subject were not controlled, it is possible that considerable changes in the daily weights might occur from these factors. The

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4. Van Slyke, D. D., and Palmer, W. W.: J. Biol. Chem. 41: 567 (April) 1920.

subjects continued their normal activity during the medication with dinitrophenol, and the only symptoms noted were a feeling of warmth and a tendency to perspire freely.

It may be concluded from the results of experiments on two normal subjects on a normal balanced diet that a 40 per cent increase in metabolism caused by dinitrophenol did not significantly modify the nitrogen or acid-base balance or cause unpleasant symptoms.

HIGH CARBOHYDRATE DIET

In the second experiment, the carbohydrate of the diet was increased to the limit of palatibility while the basal protein need of 1 Gm. per kilogram and the total caloric intake were left unchanged. This resulted in a reduction of the dietary fat to a minimum. For M. O., who weighed 74 Kg., this diet contained 2,960 calories and was made up of 533 Gm. of carbohydrate, 74 Gm. of protein and 50 Gm. of fat. For P. O., who weighed 61 Kg., the diet contained 2,440 calories and was made up of 460 Gm. of carbohydrate, 61 Gm. of protein and 40 Gm. of fat. After a week of control observations, M. O. was given 300 mg. of dinitrophenol daily for seven days and P. O. 225 mg. daily for seven days. The results obtained are presented in the chart.

The metabolism of M. O. rose from a control value of — 15 per cent to + 10 per cent on the third day, and to + 25 per cent, or a total of 40 per cent, on the seventh day of medication with the drug. In P. O. the rise was from a control value of — 5 per cent to + 50 per cent on the fifth day, and + 45 per cent on the seventh day, or a maximum increase of 55 per cent. The daily nitrogen intake for M. O. was 11.8 Gm.; the output varied from 9.5 to 13.5 Gm., an average of 12 Gm. for the two weeks. The daily intake for P. O. was 9.7 Gm.; the output varied from 6.5 to 10.5 Gm., averaging 8.8 Gm. during both control and test weeks. Thus there was no significant change in the nitrogen balance of the control and test periods. In both subjects the urinary organic acids varied between 500 and 2,000 cc. a day with no significant difference between the control and the test periods. This showed that the formation of acid bodies did not increase during the administration of the drug. M. O. lost 1 pound (0.45 Kg.) during the control period and 5 pounds (2.3 Kg.) during the medication with dinitrophenol. P. O. had an average weight of 1 pound less during the medication period than during the control period. The results in M. O. were particularly interesting, since they showed a significant weight loss without any commensurate increase in nitrogen output. This presumably indicated that the weight loss was not due to tissue destruction but to combustion of the fat or carbohydrate of the body. Subjectively, the patients felt warm and perspired easily during the medication period, but otherwise they felt quite normal.

On the whole, this experiment demonstrated that even when a maximal amount of carbohydrate or minimal fat was present in the diet the usual increase in metabolism could be produced without disturbing the metabolic functions studied or causing undesirable symptoms.

HIGH FAT DIET

In this, or the third, experiment, the dietary fats were increased to the limit of tolerance and the carbohydrates correspondingly reduced, in order to keep the caloric intake constant and the protein at 1 Gm. per kilogram of body weight. For P. A., who weighed 75 Kg., the total calories were 3,000; the carbohydrate intake was 105 Gm., the protein 75 Gm. and the fat 253 Gm. The diet of R. U., who weighed 63 Kg., contained 2,520 calories and was made up of 90 Gm. of carbohydrate, 63 Gm. of protein and 212 Gm. of fat. After a week of control observations, both subjects were given 225 mg. of dinitrophenol daily for seven days. The results are presented in the chart.

The metabolism of P. A. rose from a control value of — 15 per cent to + 15 per cent on the fifth day, and to + 35 per cent, or an increase of 50 per cent, on the eighth day after medication was started. In R. U., metabolism rose from a control value of 0 per cent to values of + 40 per cent on the sixth day and of + 30 per cent on the eighth day. The nitrogen intake for P. A. was 12 Gm. daily and the output varied from 8.5 to 15.5 Gm. during the control period, and from 10 to 14.5 Gm. during the medication period. The average of the values for nitrogen output during the control period was 12 Gm. and during the medication period 13 Gm. The differences were too small to be of significance in view of the daily variations present. R. U. showed more definitely that the nitrogen balance was maintained. Here the intake level was 10.1 Gm. and the output varied from 6.5 to 11.5 Gm. a day, averaging 10 Gm. during both the control and the medication period. The urinary organic acids showed an average of 750 cc. a day during both weeks for P. A., and 500 cc. during both weeks for R. U., again without evidence of increased acid-body production. The weights of both subjects varied considerably during the control period, but both lost 3 pounds (1.4 Kg.) during the medication with dinitrophenol. The subjects were free from pronounced symptoms, even when their basal metabolism was maximally elevated, as in all previous experiments. There was only a moderate feeling of warmth and some increased fatigability on exertion.

Thus, dinitrophenol was effective in increasing the metabolism, without disturbing the basic metabolic processes studied, although the subjects ate a diet containing an abnormally large amount of fat and a minimal amount of carbohydrate.

HIGH PROTEIN DIET

In the fourth experiment, the caloric value of the diets was maintained at 40 calories per kilogram, but the protein was increased to 1.7 Gm. per kilogram of body weight. Carbohydrate and fat were apportioned as in a balanced diet. The diet for P. A., who weighed 75 Kg., contained 3,000 calories: 300 Gm. of carbohydrate, 125 Gm. of protein, and 133 Gm. of fat. The diet for P. O., who weighed 61 Kg., contained 2,440 calories: 250 Gm. of carbohydrate, 100 Gm. of protein and 115 Gm. of fat. After a week of control observations, both subjects were given 225 mg. of dinitrophenol daily for seven days. The results are indicated in the chart.

The metabolism of P. A. rose from a control value of — 15 per cent to + 12 per cent, or a rise of 27 per cent, on the third day of medication and remained at that level. The metabolism of P. O. rose from + 10 per cent to + 50 per cent, or an increase of 40 per cent, by the fifth day of medication and remained at that level during the two remaining days of that period. The nitrogen intake for P. A. was 20 Gm. a day, but the output never reached this level. During the control period it rose to nearly 18 Gm. a day but averaged only 16.5 Gm. during the medication period. Likewise, the output of P. O. did not approach the intake level

of 16 Gm. a day until the end of the experiment, rising constantly to the end. It appears that on a high protein diet the nitrogen balance may remain positive, at least during the first week of medication with dinitrophenol. The urinary organic acids were remarkably constant throughout. In both subjects there was little variance from a value of 750 cc. a day during the control and medication periods, again showing no tendency to acidosis. Although there was some variation in body weight, the two subjects did not lose more than a pound each during the medication with dinitrophenol. The symptoms were the same as those of the other diets discussed.

Thus, when protein formed an unusually large part of the diet, the increased metabolism of dinitrophenol did not disturb the basic metabolic processes of the body and caused no unpleasant symptoms.

COMMENT

Elevations in basal metabolism caused by dinitrophenol of between 27 and 50 per cent and persisting for periods of from seven to sixteen days were studied in subjects on controlled diets. The diets were all adequate as to caloric content on the basis of a normal metabolic rate, containing 40 calories per kilogram of body weight, but were abnormal in that they contained a maximal tolerated amount of carbohydrate, fat or protein. A normally balanced diet was also used for comparison. Such diets represented the extremes likely to be encountered in the dietaries of patients receiving dinitrophenol.

Dinitrophenol, used in doses of therapeutic range, caused increases in metabolism of the usual magnitude irrespective of the type of diet. The nitrogen excretion was never greater than the intake, even when the subjects lost as much as 5 pounds in body weight during one week. From this it seemed probable that there was no actual tissue breakdown during these short periods of heightened metabolism, but that the loss of weight was due to the utilization of stored carbohydrate or fat. This does not mean, of course, that tissue breakdown would not occur if the drug should be given over longer periods, but probably when materials other than protein are available these are utilized first. Thus the assumption might be made that, as long as the protein intake is adequate, any reduction in body weight is not primarily at the expense of the tissue proteins. The failure to demonstrate any change in the amounts of acid bodies in the urine indicated that the fat burned was consumed completely and did not tend to cause an acidosis.

These results indicate that dinitrophenol may be administered to patients on special dietary regimens over short periods without interfering with the usual metabolic effects of the drug. Therefore, dinitrophenol would seem especially useful in obesity, in which, through burning of the stored fats, a reduction in body weight might be obtained. This reduction would be accompanied by a minimal destruction of body tissue, since there was no demonstrable increase in the nitrogen output. Also, because of the absence of unpleasant subjective symptoms, dinitrophenol might be valuable for increasing the depressed metabolism of various disease states. Thus, the palpitation and anxiety that often follow the administration of thyroid in sensitive patients might be avoided. This does not mean, however, that dinitrophenol can entirely replace thyroid, for there may be actions of this gland necessary or useful to the body, in addition to its power of increasing metabolism.[5] In a later paper, we expect to discuss a number of actions of thyroid not possessed by dinitrophenol.

It may be added here that no demonstrable side actions have been observed in the human subjects reported in this paper under these adverse dietary conditions. However, among a large group of patients under observation in the Stanford clinics and from reports of physicians who have tried dinitrophenol, there would seem to be an incidence of something like 5 or 6 per cent of dermatitis. Such a reaction occurs with many other drugs and promptly disappears on withdrawal of the drug. As for other side actions, such as those resulting from renal or hepatic functional injuries, nothing definite has been demonstrated thus far by us, but observations along these lines are being continued and will be reported later.

CONCLUSIONS

1. The effects of alpha-dinitrophenol (1-2-4) on basal metabolism, nitrogen balance, urinary organic acids, and body weight were studied in subjects on balanced diets and on diets unbalanced by including maximal amounts of carbohydrate, fat or protein. The dinitrophenol was administered by mouth for periods of from seven to sixteen days. The caloric values of the diets were adequate for the normal metabolism of the subjects.

2. With the use of these diets, the basal metabolism was increased by from 30 to 50 per cent during medication with dinitrophenol.

3. The subjects excreted less nitrogen than they ingested, yet there were definite losses of body weight. Therefore, body proteins probably were not broken down. The output of urinary organic acid was not increased, thus indicating that the fats were completely burned without giving rise to acidosis.

4. Accordingly, dinitrophenol may increase metabolism in man, regardless of the energy materials of the diet, although it primarily promotes burning of carbohydrates or fat, at least during short periods, such as those used in this study and on diets of adequate caloric value.

5. Clinically, dinitrophenol is indicated in treatment for obesity and may be therapeutically useful in other disease states with depressed metabolism. Its main advantages over thyroxine or powdered thyroid would seem to be a prompt and vigorous rise of metabolism and an absence of disturbing subjective symptoms. Its use appears to be relatively safe for as long periods as have been studied so far.

Sacramento and Webster streets.

5. Cutting, C. C., and Tainter, M. L.: Proc. Soc. Exper. Biol. & Med. **31**:97 (Oct.) 1933.

The Way the Patient Lies in Bed.—The fixed rigidity of meningitis is easy enough to recognize in the advanced case. Its early recognition in a case of obscure fever and headache or in subarachnoid hemorrhage may require the cooperation of the hands, but the decision to make the further test is often prompted by the appearance of unwillingness in the patient to move his head from the pillow. The adoption of the knee-elbow position by a rheumatic child may be the first sign of pericarditis. Gull once surprised an anxious mother by telling her that her daughter with typhoid fever would recover before he had entered the sickroom. He had seen her sitting up in bed as he passed the door.—Ryle, J. A.: The Training and Use of the Senses in Clinical Work, *Guy's Hosp. Gaz.* **47**:421 (Oct. 28) 1933.

PERSISTING ERRORS IN THE TECHNIC OF ORAL CHOLECYSTOGRAPHY

A PROCEDURE DESIGNED TO AVOID THEM

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A prevalent belief that the intravenous method of cholecystography is consistently and definitely superior to the oral method in diagnostic results has stimulated me to reiterate my own convictions to the contrary and to recount certain rather common errors in the oral technic which may foster the opinion that it is less reliable than the intravenous method. For a long time I accepted the view that the intravenous method was somewhat more trustworthy, although I preferred to give the dye orally as a routine and reserved the intravenous test for cases in which the oral was indecisive. However, with added experience and the adoption of an appropriate oral technic I have become thoroughly convinced that, when the oral method is properly executed, its efficiency is equal to that of the intravenous method and that adverse comparisons of the two methods are usually based on results derived from faulty oral technics.

Now it should be obvious that, to employ the oral test effectively, the dye must be given: (1) in sufficient quantity, (2) in readily absorbable form, (3) in such a manner that it will not produce undue nausea or purgation, and (4) under conditions that will not hamper its evacuation from the stomach, its absorption from the bowel or its accumulation and concentration in a normal gallbladder.

From repeated trials with varying amounts I have found it best to give sodium tetraiodophenolphthalein (tetiophthalein), the compound almost universally employed, in a uniform dose of 4 Gm. to adults. This is reduced for children in proportion to weight, but I have not found it necessary to vary the dose for small or large adults. If an amount considerably less is given the shadow of the gallbladder is likely to be faint or absent, and considerably larger doses tend to produce vomiting or purging or shadows of excess dye in the bowel which may obscure the gallbladder.

During the experimental stage of oral cholecystography, roentgenologists soon discovered that when the compound was administered in pills or capsules the masses often were not dissolved, and thus the test was vitiated. Even when the capsule or pill coating dissolved, the acid gastric juice, especially that of a fasting stomach, often combined with the exposed drug to form a viscid envelop which retarded or prevented breaking up of the mass. Thus the advantage of giving the compound in solution soon became evident, and this method is now generally employed. If the drug is dispensed in aqueous solutions, they should be freshly prepared. It has been my observation that solutions more than twenty-four hours old are likely to produce nausea.

Next in importance to assuring absorbability of the dye is to give it in such a manner that it will be palatable and well borne by the stomach. Many persons tolerate the dye in simple aqueous solution, but others find its taste disagreeable or are subsequently nauseated. Both of these objections can be largely overcome or greatly mitigated by mixing the solution with a glassful of fruit juice or carbonated water. Grape juice is widely used, and I place it first on the list from which the patient may choose.

But it is not sufficient merely to disguise the taste of the dye and dilute it with an agreeable beverage, for even when thus taken on an empty or partially empty stomach, nausea and vomiting occur too often. Hence it is the more common practice to give it in association with a meal, although customs vary as to the quantity and character of the meal and the relative time at which the compound is taken. It seems to me that the significance of these factors is not appreciated as fully as it should be. After extended trials with meals different in amount and composition, and directing the compound to be taken at different times in relation to the meal, I have settled on the fixed routine of requiring the patient to take a full meal containing a minimum of fat and follow it immediately with the dye. This is, in my opinion, the most important factor in oral cholecystography.

The element of fat in the meal deserves especial consideration. More than one examiner has been interested in the plausible hypothesis that by including a substantial amount of fat in the meal the gallbladder would be emptied and thus rendered favorable for reception of the subsequently secreted dye-laden bile. In my hands, however, a faithful trial of this procedure resulted in a marked increase of positive diagnostic errors arising from faintness or absence of the shadow when the gallbladder was normal. Apparently the fat stimulates emptying of the gallbladder during the time when filling should occur. Since fat retards evacuation of the stomach, retarded absorption of dye by the bowel may follow. Delario[1] has shown by experiments on animals that fat renders insoluble a greater amount of the dye in the small bowel. Whatever the reason, I am certain that much fat in the meal will lead to a high proportion of mistakes in diagnosis.

The possibility that physiologic variations in absorption of dye by the bowel might lead to erroneous cholecystographic interpretations is still frequently mentioned, and at the beginning I had this apprehension. Repeatedly it has been emphasized that by the intravenous method a constant amount of the compound is put directly into the blood, whereas by the oral method the amount absorbed might vary so widely as to affect the reliability of the test. Yet I have not noted a single instance in which absence or faintness of the gallbladder shadow could reasonably be attributed to deficient absorption from physiologic causes, provided no disturbing factor was introduced by the manner in which the compound was administered.

To avoid interference with absorption of the dye or with its entrance into and concentration by the gallbladder, purgatives, especially castor oil, and other medicines which affect the intestine or biliary organs should not be taken by the patient during or shortly prior to the examination. Before cholecystography made its advent, purgation was often employed to prepare the patient for roentgenography of the gallbladder, and a few examiners persist in such preparation for cholecystography. It is desirable to cleanse the large bowel, but this is best effected by having the patient employ enemas on the morning of examination.

The facts and opinions recited are not novel or peculiar to my experience. Indeed, most of them were first pointed out by other roentgenologists, and all have

From the Section on Roentgenology, the Mayo Clinic.
Read before the Section on Radiology at the Eighty-Fourth Annual Session of the American Medical Association, Milwaukee, June 15, 1933.

1. Delario, A. J.: Paths of Absorption and Excretion of Sodium Tetraiodophenolphthalein, J. Lab. & Clin. Med. 16: 329-340 (Jan.) 1931.

received wide publicity. Nevertheless, oral technics continue to be exceedingly diverse, and in many instances they violate one or more principles which seem essential to me. Many examiners still give the dye in forms that hinder its absorption, prescribe it in inadequate doses, direct it to be taken with a light meal or with one containing an excess of fats or several hours after the meal, or precede the examination with a purgative. Such lapses are often naively mentioned by sincere critics of the oral method and undoubtedly account for the disappointing results obtained. Any comparison of the two methods under these circumstances is bound to be inconclusive and inequitable. Further, I feel that, by closer attention to the details described, some of the practitioners of the oral method would be rewarded by a surprising increase in its efficiency. It is to be conceded that rigid standardization of methods retards progress, but neglect to profit from past mistakes is equally hampering.

At the Mayo Clinic for more than three years we have applied a routine which conforms to the foregoing principles. Reactions in the way of vomiting or distressing purgation have been few and in no case alarming. During the last year employment of the intravenous method was not deemed necessary in any case, and whenever reexamination was required the oral routine was repeated. Details of the procedure are as follows:

The patient receives 4 Gm. of sodium tetraiodophenolphthalein dissolved in 30 cc. of distilled water and is given the following printed instructions: "(1) At 6 p. m. eat supper of usual amount, but without eggs, cream, butter or other fats; (2) immediately after supper, empty the entire contents of this bottle (the dye) into a glassful of grape juice, stir well and drink all; (3) do not take a laxative or any other medicine; (4) at 7 o'clock next morning take a rectal injection of warm salt solution until the water returns clear, and (5) do not eat breakfast; you may drink water, black coffee, or clear tea."

Cholecystograms are made at the fourteenth and the sixteenth hour after the dye is taken, and again at the twentieth hour after the patient has taken a glassful of milk and cream in equal parts with his lunch.

For roentgenography the patient is placed in a comfortable position prone on the table, which is equipped with a flat Potter-Bucky grid. He lies with his cheek to the pillow, his arms forward and his ankles supported by a cushion. To secure thorough immobilization, a broad canvas band is drawn tightly over his back. He is required to exhale deeply and then cease breathing during the exposure. Voltage is proportioned to the patient's thickness, and the entire setting is equivalent to that which will exhibit details of bone structure. A constant target film distance of 26 inches (65 cm.) is employed, and the exposure time varies from one-half to one second.

When the first set of roentgenograms is developed, it is inspected so that technical errors can be corrected. If the shadow of the gallbladder is obscured by gas, the technician massages the abdomen to displace the gas or requires the patient to repeat the enema. If the shadow is partly hidden by the ribs, subsequent cholecystograms are made after inspiration and arrest.

The efficiency of this routine is exemplified in the results of the work during 1932. Of 4,676 patients examined, 732 were operated on, and the cholecystographic diagnosis, whether positive or negative, was confirmed in 696 (95.0 per cent). Among 287 patients with normal cholecystograms, who were operated on chiefly for diseases other than that of the gallbladder, then cease breathing during the exposure. Voltage is proportioned to the patient's thickness, and the entire setting is equivalent to that which will exhibit details of bone structure. A constant target film distance of 26 inches (65 cm.) is employed, and the exposure time varies from one-half to one second.

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Cholecystographic Data for 1932

Diagnosis	Cases	Observations at Operation: Gallstones	Tumors	Cholecystitis: Not Graded	Grade 2	Grade 3	Grade 4	Miscellaneous	Normal	Diagnosis Confirmed at Operation, per Cent
Normally functioning gallbladder	287	4	2	19	4	..	1	..	257	89.5
Poorly functioning gallbladder	39	28 (71.8%)	..	5	..	1	2	1	2	94.8
Nonfunctioning gallbladder	106	90 (84.9%)	3	4	3	..	2	1	3	97.1
Normally functioning gallbladder with stones	124									
Poorly functioning gallbladder with stones	78	294	292	1	..	..	..	..	..	..	99.6
Nonfunctioning gallbladder with stones	92									
Tumor	6	..	6	..	..	..	..	..	..	100.0
Total	732	415	12	29	7	1	5	2	262	

445 cases with positive cholecystographic data; 6 errors (98.6 per cent correct). Of 732 diagnoses, 696 (95.0 per cent) were confirmed

415 cases with gallstones at operation; 411 (99.0 per cent) with positive cholecystographic data. Of the 415 cases, gallstones were visualized and reported in 294 (70.8 per cent)

439 cases with disease of the gallbladder at operation; positive cholecystographic data in 439 (98.6 per cent)

262 cases without disease of the gallbladder at operation; negative cholecystographic data in 257 (98.0 per cent)

surgical exploration confirmed the cholecystographic diagnosis in 257 (89.5 per cent). It is well known that the highest percentage of errors is caused by diseased gallbladders which maintain their function sufficiently to produce a normal shadow. The percentage of errors in such groups would probably be increased if the intravenous method were superior in eliciting shadows of functioning gallbladders. Of 445 patients with positive cholecystographic data, 439 (98.6 per cent) had cholecystic disease. It is precisely in this group that skeptics of the oral method would expect a high ratio of errors. Gallstones were found at operation in 415 cases; 411 (99.0 per cent) yielded positive cholecystographic data and the gallstones were diagnosed as such in 294 (70.8 per cent). In six cases in which a diagnosis of tumor of the gallbladder had been made the diagnosis was confirmed, but papillomas were also found in a few cases in which this specific diagnosis had not been made.

The personal equation was scarcely a factor, for many of the interpretations were made alternately by three of my associates in the section, and I attribute these results chiefly to our specific routine. Until such percentages have been surpassed by the intravenous method, I shall continue to apply and recommend the oral method.

ABSTRACT OF DISCUSSION

DR. WALTER L. PALMER, Chicago: The accuracy of the oral method as carried out at the Mayo Clinic seems to compare most favorably with that obtained by the intravenous technic employed in other institutions. In a series of 2,000 intravenous cholecystographies reported about three months ago by Dr. Ferguson and myself from the University of Chicago Clinics, the accuracy was not as great as that described today. During the past year we have been using the oral method and are quite satisfied with the results obtained, although they are not as good as Dr. Kirklin has reported. The oral method has two important advantages: First, it is simpler and less expensive and, second, the reactions are less frequent and less severe. Now that it has been shown to be as reliable as the intravenous method, there would seem to be little reason for continuing to use the intravenous technic. Dr. Ferguson and I attempted a clinical evaluation of cholecystography. We found that the roentgen demonstration of stone was practically 100 per cent accurate. A normal visualization seemed to us to be more reliable than has been indicated in the present report. This discrepancy may be due to a difference in interpretation. In 287 cases of normal visualization, Dr. Kirklin reported finding stones or tumor in only 6 and cholecystitis of varying grades in 24. Considerable difference of opinion exists as to the pathologic diagnosis of cholecystitis. It is possible, according to our conception of cholecystitis, that we should have classified some of these as normal gallbladders. This might account for our attributing a higher accuracy to a normal visualization. A nonfunctioning gallbladder was found by us to be indicative of cholecystic disease in about 90 per cent of our cases when it was accompanied by a history of colic, but the accuracy was much less when there was no clinical evidence of gallbladder disease. Dr. Kirklin reports an accuracy of 97 per cent entirely irrespective of the clinical picture. From the clinical standpoint it is well to recognize that stones may be present in what appears to be a perfectly normal gallbladder roentgenologically and, conversely, that a poorly functioning or a nonfunctioning gallbladder may be perfectly normal. The final diagnosis, in my judgment, must be based on both clinical and roentgenologic evidence. I should like to ask Dr. Kirklin how frequently he finds reexamination advisable, and just what he considers to be the indications for it.

DR. ADOLPH HARTUNG, Chicago: I should like to ask the author whether he makes any attempt as a routine to make an opaque meal examination in connection with the dye test. Before the dye test was used as frequently as it is now, a good deal of reliance was placed on the secondary gastrointestinal examination in connection with gallbladder disease. Since that time most of these cases, I believe, are not checked up by such an examination. In quite a large number of cases in which the dye test was made as a routine procedure, the results were negative and an opaque meal was given for secondary signs. It seems to me that the percentage of error, especially in the cases of cholecystitis, might be brought down considerably by checking up in some way such as this. I have found in connection with normal gallbladder shadows that the meal gives some of these secondary signs, either functional or organic, indicating adhesions or gallbladder disease, so that the percentage of error could be brought down materially.

DR. PAUL C. HODGES, Chicago: Until a few years ago I used the intravenous method almost exclusively, but one or two serious accidents with it caused me to change to the oral method. I supposed that the change was temporary until the difficulties could be overcome with the intravenous injection; but, as so frequently happens, I have drifted along into a permanent arrangement without being particularly careful to be sure that the oral dye was being given in the best possible fashion. From what Dr. Kirklin says, it is obvious that I have been making some mistakes. He uses 4 Gm. of dye, and I have been giving only 3 Gm. He takes pains to put the patient in a comfortable position and has him suspend respiration in the expiratory phase. I have not paid much attention to the patient's comfort and have had him hold his breath on inspiration. Dr. Kirklin has the patient reach up and hold his own nose, which I suspect is a very helpful maneuver in assuring suspended respiration. I have had an attendant hold the patient's nose in particularly difficult cases, but I do this as little as possible because I don't like to expose the attendants to the rays. The importance of complete immobilization cannot be overemphasized, and so Dr. Kirklin's efforts directed to that end are of great practical importance. I have had a little experience with rapid stereoscopic exposures made with the patient standing in front of a vertical casette changer, a Lysholm stationary grid interposed between him and the film. Films of this sort hold great promise. I should like to know whether Dr. Kirklin is using the pure dye or one of the commercial preparations containing a vehicle and flavoring matter.

DR. H. A. OLIN, Chicago: I think that I have had better success using the pure salt and dissolving it in water and mixing it with grape juice. In the event that the patient is unable to take grape juice, I use any fruit juice, because it is the acid in the fruit juice that precipitates the salt, which is redissolved when it enters the duodenum. Recently I have been interested in the complication of diarrhea. It occurred to me that giving camphorated tincture of opium with the dye would overcome this objection. I think that in the controversy about oral and intravenous methods one important matter has been overlooked, and that is the chronically inflamed gallbladder, which is out and out clinically a surgical case. I think that Graham's appreciation of the use of the liver test combined with the salt should not be overlooked. That is called iso-iodeikon (phentetiothalein sodium) and I suppose it is as familiar as iodeikon (sodium tetraiodophenolphtnalein). By ascertaining the liver index one is able to obtain the amount of liver damage and the degree of operative risk many days prior to operation. I agree with Dr. Kirklin that the fat meal is of decided advantage, especially to show when the gallbladder is almost completely empty or partially empty. Last month I observed three gallbladders which appeared normal in a cholecystogram. These were three strawberry gallbladders, and I should like to ask Dr. Kirklin whether he has had a similar experience.

DR. B. R. KIRKLIN, Rochester, Minn.: I have reported only cases which have been checked pathologically with the exception of those cases in which the operation was for other abdominal conditions and the gallbladder was merely palpated or inspected and determined to be normal and therefore not removed. Some one has asked regarding the indications for reexamination and what percentage of the cases are reexamined. The indications for reexamination are unsatisfactory films or any doubt that the patient has followed instructions. Approximately 8 per cent of the total number of the cases are reexamined; the dye is usually repeated the night following the first examination. In reviewing those cases in which a normal functioning gallbladder has been reported and small stones have been found, it has invariably been learned that the cause of the error has been an attempt to interpret films of inferior quality in that there was movement on the part of the patient or gas in the overlying segment of bowel, which obscured the stone shadows. I feel that if one has satisfactory cholecystograms and the gallbladder is functioning normally, stones can invariably be ruled out. As evidence of the importance of meticulous technic in cholecystography, the percentage of accuracy has increased hand in hand with the improvement in technic. I have not followed the method of examining the stomach and gallbladder on the same day; I prefer to make cholecystograms on the day preceding examination of the stomach, although I can see no reason why they cannot be made the same day. Dr. Hartung mentioned the diagnosis of gallbladder adhesions, which brings up a very important question. I have little confidence in my ability to diagnose gallbladder adhesions. Early in this work I thought I could recognize adhesions by deformities of the gallbladder contour, but I have since learned that there is no relation between adhesions and deformity of the gallbladder wall in cholecystograms, nor does a smooth gallbladder contour rule out adhesions, in my experience. Dr. Hodges has asked what dye is used; for some time I have employed sodium tetraiodophenolphthalein and have found it a most satisfactory preparation. I do not use camphorated tincture of opium as a routine but I can see some advantages in its use. Some one has asked regarding the strawberry gallbladder. I have found that the cholecystograms of an uncomplicated strawberry gallbladder will almost invariably show that it is functioning normally.

STIFF, PAINFUL SHOULDERS, EXCLUSIVE OF TUBERCULOSIS AND OTHER INFECTIONS

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This article is limited to: (1) the enumeration of a number of terms for stiff, painful shoulders with practically the same clinical syndrome; (2) an analysis of the pathologic changes found in dissections, autopsies and operations; (3) a study of the rôle that rupture of the supraspinatus tendon, capsule and subacromial bursa plays as an etiologic factor; (4) a review of a few cases to emphasize the importance of apparently trivial symptoms, usually overlooked or neglected as unimportant; (5) a brief outline of the essentials of treatment, based largely on a study of 340 shoulders in dissecting rooms; (6) a description of a simplified operation for tendon and capsule repair.

In particular, my purpose is to direct attention to evidence that rupture of the supraspinatus tendon is apparently the primary exciting cause of most "stiff, painful shoulders," and that an early recognition of that fact, with prompt proper treatment, will bring about much earlier and better end-results.

Duplay,[1] three score years ago, described an involvement of the subacromial bursa from trauma, and named this condition "scapulo-humeral periarthritis." Dickson and Crosby[2] used the term "periarthritis of the shoulder" in their recent analysis of 200 cases. And Codman,[3] a pioneer in research work on the shoulder used "rupture of the supraspinatus tendon," believing such a term to be descriptive of a constant part of the pathologic process found in these shoulders. Royal Whitman[4] used the term "stiff, painful shoulders" and "periarthritis of the shoulder" synonymously.

In the evolution of the shoulder from a walking, weight-bearing joint to a weight-carrying one, much strength, stability and durability have been lost. The shoulder joint has the greatest range of motion and the most extensive moving capsule, and, relatively, the glenoid has the smallest, shallowest joint socket. Such a joint is particularly prone to injury, so that it is not surprising that Codman found a complete rupture of the supraspinatus tendon to every twenty shoulders examined, and one incomplete rupture to every third shoulder. In a study of 340 shoulders, my observations were 1 complete rupture of the supraspinatus tendon to every 28 shoulders examined, and 1 incomplete rupture to every 6 shoulders.

The complete ruptures showed much fraying of the tendon and almost no signs of repair, while seventeen of the forty-four incomplete ruptures of the supraspinatus tendon had healed, nearly closing the rupture gap. Had all the incomplete ruptures been immobilized with the arm well elevated, it is my belief that there would have been sufficient approximation in the entire forty-four to result in a satisfactory healing of the damaged tendons and contiguous structures.

Deposits were found in more than a third of the cases of rupture. These deposits were in and about the supraspinatus tendon, as stressed by Brickner,[5] Codman, Moschcowitz[6] and others. It was a significant fact that practically all of the gross pathologic changes found were in and about the ruptured supraspinatus tendon. Furthermore, in the absence of tears of the tendon, practically no degenerative changes, such as fatty, chalky or putty-like deposits, were found. Apparently, rupture was the first link in the chain of pathologic changes.

Dickson and Crosby, "in an effort to elucidate the relationship of trauma, foci of infection and metabolic factors in the etiology," concluded that "there must be some common denominator, which cannot be accounted for at present." In the light of Codman's and my own research, that "common denominator" may be rupture, much or little, of the supraspinatus tendon. The rupture, almost universally overlooked, for reasons to be given later, may be and probably is the primary exciting cause, and inherent structural weakness of the shoulder, a poor blood supply, metabolic factors and foci of infection are secondary, though important, once a rupture has occurred.

Fig. 1.—Landmarks of the shoulder: *A* (dotted line), the incision for exploratory operation; *B*, extensions of the incision for repair of the capsule and tendon; *C*, the circumflex artery and nerve which lies between the humerus and the deltoid, with branches entering the muscle; *E*, the acromion; *F*, the clavicle.

Codman believes that virtually every rupture of the supraspinatus tendon is caused by contraction of the supraspinatus muscle and that tears are rarely produced by direct trauma. For the most part, I concur

From St. Francis Hospital.
Read before the Section on Orthopedic Surgery at the Eighty-Fourth Annual Session of the American Medical Association, Milwaukee, June 16, 1933.

1. Duplay, Simon: Arch. gén. de méd., Paris **2**: 513, 1872.
2. Dickson, J. A., and Crosby, E. H.: Periarthritis of the Shoulder, J. A. M. A. **99**: 2252 (Dec. 31) 1932.
3. Codman, A. E.: Boston M. & S. J. **150**: 371, 1904; **154**: 613, 1906; **159**: 533, 576, 615, 677 and 723, 1908; **164**: 708, 1911; **165**: 115, 1911; **196**: 381, 1927; Surg., Gynec. & Obst. **52**: 579, 1931.
4. Whitman, Royal: A Treatise on Orthopedic Surgery, Philadelphia, Lea & Febiger, 1930.
5. Brickner, W. M.: Am. J. M. Sc. **149**: 351, 1915; Am. J. Surg. **30**: 168, 1916.
6. Moschcowitz, Eli: Am. J. M. Sc. **150**: 115, 1915.

in that belief. Occasionally, a dislocation of the shoulder is accompanied by a tear of the tendon and capsule; for example, two such cases were found in my work, and Wilson [7] reported one case. Other cases are as follows:

One of Wilson's patients produced a complete rupture of the tendon in an attempt to toss a stone up out of a trench. Another was pulling down on a chain hoist; his hand slipped, and in his effort to regain his balance, violent action of the supraspinatus muscle ruptured the supraspinatus tendon.

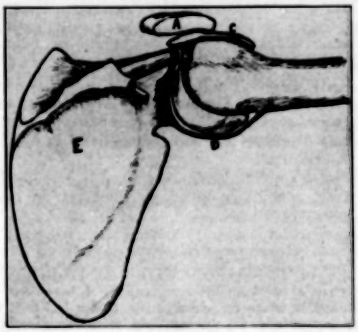

Fig. 2—*AA* represents the section of acromion removed; *B*, the supraspinatus tendon; *C*, the subacromial bursa; *D* the lower portion of the capsule; *E*, the infraspinatus fossa with the infraspinatus muscle and tendon removed.

One of Codman's patients produced a rupture in an effort to recover his balance, when a saddle girth he was tightening suddenly broke.

One of my patients, a middle-aged woman, slipped as she stepped onto an oiled floor. As her feet shot forward, she raised her arms to regain her balance and thus ruptured the right supraspinatus tendon.

Another patient, a young man of 24, not accustomed to hard work, undertook the task of passing up cases of soda pop. After six weeks of this hard labor, which put the supraspinatus tendon to constant strenuous use, he noticed one evening after work a dull, aching pain in the right shoulder. He was unable to resume his work because of pain and disability. When I saw the case six months later there was limitation of abduction with extreme atrophy of the spinatus muscles. A coarse, crunching crepitus was felt about the greater tuberosity as it approached the acromion. Pain and tenderness were present in the same area. It would appear that repeated sprains, i. e., rupture of a few fibers at a time, had occurred till at the end of six weeks the entire tendon was torn from its attachment. In this case, now over two years old, the patient has not been operated on, though Wilson operated in a similar case in which the patient produced piecemeal, by his routine folding of cloth, a complete rupture of the supraspinatus tendon.

Another patient of mine, a middle-aged blacksmith, in starting down to the cellar lost his balance, and in his effort to regain his equilibrium the sudden contraction of the spinatus muscles ruptured his supraspinatus and infraspinatus tendons, making a gap 2 by 2½ inches (5 by 6.3 cm.) through which the head of the humerus appeared at operation.

The history in conditions of the shoulder is of extreme importance, and in taking it, the most painstaking inquiry as to every possible detail from many angles will, with surprising regularity, disclose that there has been a sudden stress on the spinatus tendons or that there has been long-continued overuse.

A surprising and misleading fact is the little or no pain noticed at the time of the rupture, whether the latter occurs at once or piecemeal, as in the cases described. The pain has a sticking or cutting quality and lasts but a moment, so that the incident is usually forgotten. Some hours may elapse before aching and disability set in, dependent somewhat on the extent of the trauma. When there is extensive rupture, few patients complete the day's work. At night the pain is much worse, often preventing or interrupting sleep. On abduction, pain is usually cutting as the arm nears the horizontal, and the patient may drop his arm to the side, owing in part to weakness and in part to pain. Pain is complained of in the deltoid area, and it may radiate up or down. Tenderness is often less marked the first two or three weeks than later. It is usually elicited around the greater tuberosity, particularly proximal to its upper border. In complete rupture of the supraspinatus tendon, well marked atrophy of its muscle has been observed as early as two weeks after the rupture occurred.

Ridlon [8] confessed, "that the difficulties encountered in treatment of injuries to the shoulder joint have always been more troublesome and more obscure than the difficulties in treating all other joints put together." Lovett [9] once said: "No common injury is so badly treated, save possibly the spine, as injuries to the shoulder." Part of the reason for this unsatisfactory treatment would seem to be a lack of recognition of the fact that seemingly trivial trauma may, and frequently does, produce a tear in the structures of the shoulder joint, and that the tear is often accompanied by little or no pain. This lack of recognition has come about, in part, because shoulders are rarely operated on for relief, and painful shoulders, not being fatal, provide no autopsies.

However, because of the astonishing number of ruptures found in routine examination of shoulder joints by Codman and myself, it would seem justifiable, in cases of stiff, painful shoulders not greatly improved in two or three weeks by immobilization in abduction,

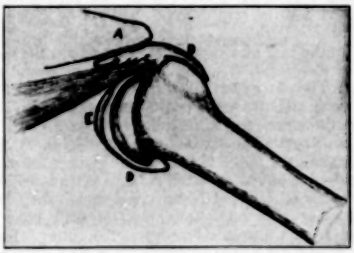

Fig. 3.—*A* is the acromion; *B*, the subacromial bursa; *C*, the partially ruptured and frayed supraspinatus tendon, capsule and subacromial bursa; *D*, the capsule; *E*, the glenoid cavity.

to assume that a rupture has occurred. Of course, along with the local treatment, a careful general examination and treatment of any abnormality, such as diabetes, gout, hyperthyroidism or hypothyroidism and foci of infection, should not be neglected.

In cases where a steady, marked improvement has not occurred during the first three weeks it is my belief that an exploratory operation should be done under

7. Wilson, P. D.: Complete Rupture of the Supraspinatus Tendon, J. A. M. A. **96**: 433 (Feb. 7) 1931.

8. Ridlon, John: Surg., Gynec. & Obst. **54**: 553, 1932.
9. Lovett, R. W.: Surg., Gynec. & Obst. **34**: 437, 1922.

local anesthesia to settle the diagnosis and to insure comparatively early proper treatment.

OPERATION

Step 1 is performed under local anesthesia to confirm or refute the diagnosis; step 2, under general anesthesia to repair the rupture.

1. The exploratory incision starts over the acromion, ¾ inch (2 cm.) back of its tip, and extends distally

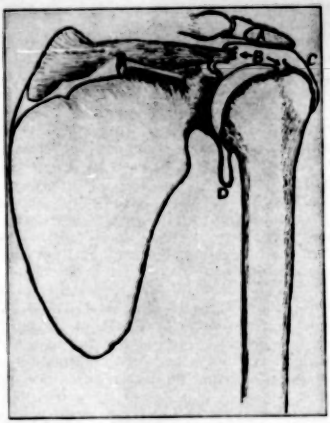

Fig. 4.—*AA* is the sector of acromion removed; *B*, complete rupture of the capsule, subacromial bursa and supraspinatus tendon with wide separation; *C*, the subacromial bursa with a wide opening into the shoulder joint; *D*, the dependent capsule.

2 inches, parallel to the fibers of the deltoid muscle. The deltoid fibers are separated, and the underlying subacromial bursa is opened. If the floor of the bursa is intact there is no rupture, in which event the incision is closed, and the convalescence will not be appreciably delayed.

2. In the case of a rupture needing repair, the second step of the operation is continued under a general anesthetic: The outer end of the incision is extended 1 inch (2.5 cm.) and the inner end 2 inches. The acromion is cut through from without inward, starting ½ inch (1.2 cm.) back of the acromioclavicular joint. A gutter is cut along the upper border of the greater tuberosity, and the edge of the retracted rupture is trimmed, while the clavicle is retracted forward. Through the base of the greater tuberosity four or five drill holes are passed from without, emerging in the gutter. Strong linen or silk on a curved needle is passed from without through hole 1, then through the torn tendon and back through hole 2. A second suture is passed similarly through hole 2, then through the tendon and back through hole 3, and so on, till all the sutures are placed. The sutures are then tied, while the arm is elevated. The bone springs back into place as soon as traction is withdrawn. A few buried sutures are inserted and the skin is closed with a continuous dermal suture. The arm is put up, well abducted, on a light supporting splint for two weeks and then is placed in a sling. The patient is encouraged to use the arm as soon as the soreness from the operation subsides.

SUMMARY

1. Stiff, painful shoulders, periarthritis of the shoulder, subacromial bursitis and rupture of the supraspinatus tendon are not strictly independent entities. They are the links in the chain of pathologic changes found in chronically disabled shoulders.

2. Rupture of fibers of one or both spinatus tendons, with the inevitable injury of the capsule and subacromial bursa, is the beginning of most pathologic processes in the shoulder, which progress needlessly because of hazy diagnosis and poor treatment.

3. The great frequency and abundance of pathologic change found in routine dissection of shoulders indicates that it is largely overlooked and, for the most part, not even suspected in cases of disabled shoulders.

4. Early diagnosis and consequent proper treatment will make operative treatment of incomplete ruptures rarely necessary.

5. Late diagnoses and late operations mean relatively poor end-results.

6. The operation herein described seems to have advantages over other operations for repair of one or both spinatus tendons.

ABSTRACT OF DISCUSSION

Dr. Edwin W. Ryerson, Chicago: Dr. Fowler has done a fine piece of work in his investigation. I have seen very few patients in whom the supraspinatus tendon had been torn. I have seen several old cases in which operation would not have been advisable and have refused to operate. Two weeks ago I saw a boy who had a reasonably recent tear which was easily demonstrable because a little piece of the greater tuberosity had been torn off. I think that operation should be done in this case but I question very much whether the old chronic tears will give good enough results after operation to make it worth while. I have done none in the old cases. The cases presenting the masses of gritty, calcareous matter, either in the supraspinatus tendon or, as I think in some cases, in the bursa, sometimes require operation and sometimes do not

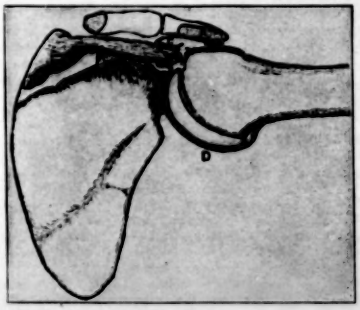

Fig. 5.—*AA* is the sector of acromion removed; *B*, complete rupture (as in fig 4), almost approximated by elevation of the arm; *C*, the subacromial bursa; *D*, the lower portion of the capsule.

Dr. F. J. Gaenslen, Milwaukee: Dr. Fowler has done an excellent service in further elucidating the subject of stiff and painful shoulders. I enjoyed especially his collection of anatomic specimens in the Scientific Exhibit. One cannot but be impressed with the correctness of Dr. Codman's and Dr. Fowler's statements that the injury is of relatively frequent occurrence. I cannot explain the fact that so few cases are seen with marked late disability in the absence of operative repair or adequate conservative treatment at the time of the injury. The gradual fraying of the supraspinatus tendon by repeated

minor injuries, associated with overuse of the arm in abduction, is apparently not unusual, although more severe single traumas undoubtedly are responsible for the majority of actual tears. A few years ago, while I was in Boston with a small group of Wisconsin surgeons, Dr. Codman discussed this problem for us at length. I remember his saying that the diagnosis of bursitis is perhaps no more justified than a diagnosis of peritonitis. Differentiation of the cases into actual rupture, complete or incomplete, calcified deposit in the tendon, or chronic adhesions should be possible in the great majority of cases.

DR. EDSON B. FOWLER, Evanston, Ill.: In regard to Dr. Ryerson's hesitancy to operate in old cases, it is well to state that Codman and Wilson reported old cases. Twenty per cent of the patients were able to resume their former occupations. In 80 per cent the condition was more or less improved and the patients were able to do a variable amount of light work. The operation as performed by Codman or Wilson gives sufficient lysis of the capsule and tendon to permit adequate closure of the rupture gap. In the old cases it is necessary to incise the capsule along the anterior and posterior borders of the tendon, as well as under the tendon where it leaves the capsule. This permits the suture of the retracted structures to the greater tuberosity with a good closure of the rupture gap. Very rarely, deposits are found in the subacromial bursa, as stated by Dr. Ryerson and as found by myself and others. The piecemeal ruptures and associated erosions noted by Dr. Gaenslen are far more common than the sudden complete rupture of the tendon and associated capsule and bursa.

USE OF PHENYLMERCURIC NITRATE IN TINEA AND YEAST INFECTIONS OF THE SKIN

PRELIMINARY REPORT

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CLEVELAND

During the past three years, Weed and Ecker[1] reported on two new mercurials showing unusual bactericidal and fungicidal properties coupled with low toxicity for man and animals. Of chief interest and importance was phenylmercuric nitrate.

They studied the effect of phenylmercuric nitrate on twenty pathogenic fungi of man and it was shown that with the exception of Achorion violaceum all the implanted fungi failed to grow in mediums containing 5 and 1 per cent of the saturated solution of phenylmercuric nitrate. Subcultivation on new mediums proved that the majority were killed, since only two (Trichophyton acuminatum and Achorion violaceum) from the medium containing 5 per cent saturated solution of phenylmercuric nitrate grew. However, from the medium containing 1 per cent five subcultures showed growth. They also showed that phenylmercuric nitrate readily killed six strains of wood-destroying fungi. Hatfield,[2] one year later, corroborated the fungicidal value not only of phenylmercuric nitrate but also of phenylmercuric chloride.

The high bactericidal efficiency of phenylmercuric nitrate has also been confirmed experimentally by Birkhaug [3] and clinically by Biskind.[4]

At the suggestion of Dr. E. E. Ecker, the effectiveness of this compound (phenylmercuric nitrate) was studied in the treatment of fungous and bacterial infections of the skin.

From the outpatient department, Mount Sinai Hospital, Cleveland.

1. Weed, L. A., and Ecker, E. E.: J. Infect. Dis. **49**:440 (Nov.) 1931; **51**:309 (Sept.-Oct.) 1932; **52**:354 (May-June) 1933.
2. Hatfield, J.: American Wood Preservers Assn. Annual Report, Jan. 26, 1932.
3. Birkhaug, K. E.: J. Infect. Dis. **53**:250 (Sept.-Oct.) 1933.
4. Biskind, L. H.: Surg., Gynec. & Obst. **57**:261 (Aug.) 1933.

FORMS OF MEDICATION

As it was necessary to determine an efficient concentration of the drug for dermatologic use and to find an effective vehicle, a number of mixtures were prepared and employed. The optimum concentration was derived in the following manner: A lotion consisting of phenylmercuric nitrate 1:1,000 in an emulsion of gum tragacanth was used. The product was highly efficient but its continuous application proved to be moderately irritating to the skin, owing either to too great an original strength of the emulsion or to evaporation and resultant concentration. A lotion was then prepared containing phenylmercuric nitrate in a dilution of 1:1,250. This was decidedly less irritating. Application of a simple aqueous solution of phenylmercuric nitrate 1:1,250 by itself produced good results, but the possibility of drying contraindicated its use. Subsequently, an ointment was prepared consisting of equal parts of wool fat and an aqueous solution of phenylmercuric nitrate 1:1,250, the solution being gradually added to the lanolin in the course of emulsification in an electrical mixer. In general, this ointment containing the drug in a concentration of 1:2,500 proved more satisfactory than the lotion. After further experimentation an ointment was made containing the phenylmercuric nitrate in a concentration of 1:1,500 by weight with the addition of 10 per cent of glycerin. This ointment proved to be most satisfactory. A 1:1,000 concentration again proved too irritating for general uses. The ointments found to be most efficient were made with two hydrophilic bases containing cholesterin derivatives. Both these ointment bases containing phenylmercuric nitrate in a dilution of 1:1,500 gave excellent results and showed apparently better penetrating properties. They were unquestionably superior to the ordinary hydrous wool fat preparations.

METHOD OF APPLICATION

The patient was instructed to cleanse thoroughly all affected parts prior to the use of the ointment or lotion. This was done by means of soap and water and a soft brush. A moderate amount of one of the mixtures was gently rubbed into the infected area twice daily, night and morning. Overtreatment was avoided.

NUMBER OF CASES

Of 262 cases studied, 205 were carefully followed up and the patients discharged as cured. The remaining 57 patients were seen but once after the beginning of treatment and the data in these cases remained incomplete. Of the 205 patients, 193 had tineas and the remaining 12 had interdigital saccharomycosis.

INTERDIGITAL SACCHAROMYCOSIS

It has been a common experience among dermatologists to find interdigital saccharomycosis unresponsive to therapy. For this reason special attention was paid to this type of infection, because favorable therapeutic results would here definitely establish the value of the drug. The results obtained with both the lotion and the ointment proved that they were efficient in the treatment of this intractable infection, twelve out of fourteen patients being cured and the other two markedly improved. Occasionally the lotion proved superior to the ointment. The length of time necessary to effect the cure varied from two days to four weeks, with an average of two weeks. One patient, cured in two days, used a lotion in the dilution of 1:1,000.

The outstanding case was that of Mrs. K. K., who had had the infection constantly for twelve years.

During this time she was under continuous treatment with various forms of medication, such as tincture of iodine, 5 per cent aqueous solution of copper sulphate, Whitfield's ointment and an ointment containing oil of cassia, oil of cloves and iodine, without results. Phenylmercuric nitrate ointment 1:1,000 was tried and found to be somewhat irritating. A few days later she was given a 1:2,000 ointment, which did not irritate. There was a complete cure in two weeks with no recurrence in three months.

Two of the patients had recurrences, one of whom has since been cured and the other of whom is now under treatment. Usually there was complete relief of pain and pruritus after one application.

TINEAS

Of the 193 cases of tineas treated, all were cured. There was a total of 110 patients with tinea of the feet, 21 of whom had a secondary epidermophytid of the hands. In each instance the epidermophytid cleared up promptly, usually before the tinea of the feet was cured. One of the cases of epidermophytid of the hands showed the importance of proper differentiation between the primary infection and the secondary allergic reaction. This patient presented a vesicular scaly eczematoid eruption on both hands of seven years' duration. At no time were the hands free of this eruption, being worse at certain times than at others. Examination of the feet when first presented showed no apparent disease. After three weeks with phenylmercuric nitrate ointment 1:2,000 applied twice daily to the hands, there was no improvement. The ointment was discontinued and roentgen therapy instituted. The first treatment caused most of the lesions to regress. Further treatments, however, aggravated the lesions. A total of 2 skin units was given. One week after the last roentgen treatment, when the hands were at their worst, the patient's feet were reexamined. They showed some fissuring and scaling under each of the little toes. The patient was instructed to apply the ointment on her feet only. Four days later her hands and feet were both healed. There has been no relapse in a period of over five months. Similar results were obtained in other cases with epidermophytid or trichophytid eruptions. In each instance the treatment of the primary focus relieved the patient from the secondary eruption.

Twenty patients with tinea of the hands were treated. All of these were cured. They did not show involvement of the feet.

Of the twenty-four patients with tinea cruris, all were cured by the use of the 1:1,500 ointment.

Five patients suffered from tinea of the anal region. The outstanding feature was the relief from pruritus noted usually after one application of the ointment. The same is true of pruritus vulvae. However, further investigation of a larger series of these cases is necessary.

E. G., a man, aged 36, had severe pruritus ani due to tinea for the past few years. During this interim he was seen by several physicians, one of whom gave him seven roentgen treatments. Roentgen therapy produced temporary relief lasting from one to four months. He also had used 2 per cent salicylic acid in alcohol and later a modified Whitfield ointment. The latter treatment gave him partial relief only and later no relief at all. When seen, he was exhausted and had lost considerable weight from lack of sleep caused by the severity of the pruritus. The anal region and intergluteal cleft were macerated, excoriated and infiltrated, the process extending down over the perineum to the scrotum. When the patient was seen three weeks later, the tinea was completely cured. The pruritus, he reported, disappeared after several applications of the ointment. There was no recurrence ten months later.

Five cases of tinea of the axillary regions were treated with complete relief. In one case the 1:1,000 lotion proved to be superior to the ointment.

Tinea circinata of the glabrous skin presented an interesting series. Twenty-one cases were studied occurring between the ages of 1 and 60 years. The most interesting case was that of Mrs. W., who had a generalized tinea corporis of seven or eight years' duration. A large variety of ointment and roentgen therapy had been used to no avail. The x-rays were used to the extent that it was feared that any further irradiation might cause an atrophy. Within three weeks the patient was completely cured by a 1:1,250 lotion of phenylmercuric nitrate. Another patient showing an extensive tinea circinata of the arms and legs responded more readily to the lotion than to the ointment. Most of the patients were treated with the ointment. The time necessary to effect a cure varied from three days to one month; as a rule, ten days was sufficient.

Tinea versicolor responded more favorably to the lotion than to the other preparations. All six cases seen cleared up with the lotion in the dilution of 1:1,000. As a rule, this type of tinea responds in from three to seven days.

So far, the number of cases of tinea of the scalp and face treated with phenylmercuric nitrate are too few to justify any definite conclusion. One case of tinea of the scalp was cured after two or three months of treatment. Four other patients, on returning at the end of one week, showed definite improvement. One case of tinea barbae was cured in ten days.

The majority of our cases were gathered from the dispensary and a considerable number of cases consisted of physicians and their families. It was among these that the most startling and satisfactory results were obtained because of more intelligent and consistent use of the drug. Many of our dispensary patients obtained relief and failed to return, while others used the drug spasmodically. These facts also account for the longer duration of the treatment in these cases.

It is necessary to point out that occasionally patients sensitive to mercury are encountered who receive mercurial burns from this treatment. All those seen in this series (seven) were readily relieved by the use of a bland ointment.

CONCLUSIONS

1. In a series of 262 cases of tinea and yeast infections of the skin, phenylmercuric nitrate in ointment or lotion form was used. Two hundred and five cases were cured; the remaining fifty-seven cases were definitely improved but these were not followed to completion of treatment.

2. Phenylmercuric nitrate proved highly efficacious in the treatment of these cases, producing cures when other standard medicaments had failed.

3. In the great majority of cases, no untoward results have been seen from its continued use. In the occasional

cases in which irritant effects occurred, these cleared up readily on withdrawal or on substitution of a less concentrated mixture.

4. All the phenylmercuric nitrate used in this series of cases was prepared by Dr. Ecker and conforms to his specifications.

5. Phenylmercuric nitrate is presented as a distinct contribution to the dermatologic armamentarium.

TUBERCULOSIS AMONG NEGROES

SOME OF THE PROBLEMS THAT COMPLICATE ITS CONTROL

C. St. C. GUILD, M.D.
NEW YORK

A comprehensive review of the literature dealing with tuberculosis among Negroes, and conferences with many of the outstanding men who are interested in this problem, indicate that control measures are complicated by a lack of definite information on several points of fundamental importance, which often reveals itself in a multitude of conflicting opinions.

The present status of knowledge on several of these points will be briefly discussed in the light of recent contributions, consideration being given to the extent to which control measures appear to be handicapped by lack of definite information.

DO NEGROES HAVE A RACIAL LACK OF RESISTANCE AGAINST TUBERCULOSIS?

A vast amount of literature has been written on whether Negroes have a racial lack of resistance against tuberculosis. In general, it may be said that the majority of authors are of the opinion that they do, but many publications, particularly those of former years, appear to be based on conjecture rather than fact. Within the past year, three very interesting contributions have appeared dealing with this racial factor.

In view of Bogen's statement that "an investigation of the fate of a group of patients known to have been already infected with the tubercle bacillus and living under approximately similar conditions may shed some further light upon the problem of racial susceptibility to the disease," special interest attaches to a study by Dr. Taliaferro Clark of some 6,000 hospitalized veterans, a group somewhat removed from the cloud of economic conditions and in which he believes the two races are economically equal. The study showed that "upon final disposition of the cases admitted while the disease was in a moderately advanced stage, 50 per cent of the colored and 70 per cent of the white patients showed improvement, quiescence, arrest or apparent arrest, while 39 per cent of the colored as compared with 17 per cent of the white patients died while in hospital." Dr. Clark points out that while in these economically equal groups the Negro death rate is double that of the white, in unselected population groups it is usually three or four times as high. His conclusion is that "the race factor is working in combination with the economic one against the Negro."

Pinner and Kasper, reiterating that "probably the only definitely established fact about immunity is the diminution of spread in a sensitized organism as compared with a nonsensitized one," proceed to show from postmortem examination of 303 Negroes and 219 white patients dead of tuberculosis that:

1. Hematogenous spread occurs twice as often in Negroes as in white persons.

2. Spread by way of the lymphatics occurred nearly seven times as frequently in the Negro as in the white group, whereas isolated phthisis was present in nearly half the white patients and in less than 3 per cent of the Negroes.

These authors, while recognizing the fact that environmental conditions are one of the most important factors causing the high incidence of tuberculosis among Negroes, believe that there is also a true racial difference.

Dr. F. C. S. Bradbury, in his investigation of incidence of tuberculosis in certain Tyneside districts, found a greater incidence of tuberculosis in the Irish than in the English. Even when such factors as poverty, overcrowding and large families were controlled, he concluded that "there is evidence of a racial factor which is responsible in part at least for the relatively high incidence of tuberculosis in the Irish."

Now just what do the various authors mean by a racial factor? Clark and Bradbury are not specific on this point. Pinner and Kasper have in mind a true genotypic difference (anatomic or physiologic). Most of the earlier authors and many of the more recent ones, however, when they refer to a racial factor, mean, to quote Grandy, for example, "the result of the Negroes' relatively short period of contact with tuberculosis." As Reuter points out, lack of experience with a disease is a historical and not a racial or biologic fact. Race has nothing to do with it, since two groups of the same biologic ancestry would show similar relative differences in immunity to a disease if through a series of generations one had been exposed to its selective efforts and the other isolated from its attack.

It would appear, then, that while conclusive proof is lacking the weight of opinion and evidence indicates that in addition to his environmental and economic handicaps the Negro has a lack of resistance to tuberculosis, which may be due to a true biologic difference or merely a present expression of unlike historical experience.

While accurate information as to this lack of resistance would be of the utmost interest, it would probably have but little effect on control measures. To change the anatomy or physiology of the Negro would be a difficult undertaking, and only time can correct his lack of historical experience. In the meantime, however, the importance of his environmental and economic handicaps is universally recognized, and this must obviously be the point of attack.

WHAT IS THE MOST EFFECTIVE TUBERCULOSIS CONTROL PROGRAM FOR THE SOUTHERN STATES WITH THEIR LARGE NEGRO POPULATION AND LIMITED FINANCIAL RESOURCES?

Not only is the Negro handicapped in his fight against tuberculosis by his low economic status, both as an individual and as a race, but the fact that the majority of the Negro population is concentrated in a relatively small number of states, whose financial resources are meager, still further complicates the problem of control.

Despite the large northern migration that occurred during the period 1915-1930, nine million Negroes (or,

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roughly, three fourths of the Negro population) still live in the following thirteen states, all essentially Southern: Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, Missouri, North and South Carolina, Tennessee, Texas and Virginia.

Eight of these states have more than half a million Negroes each, and in nine of them Negroes constitute more than one fourth of the total population.

Even granting the argument advanced by sociologists that with the return of prosperity this trend to the large cities of the North will be resumed, it is evident that for a long time to come the vast bulk of the Negro population will be found in the group of states just enumerated.

Furthermore, of the nine million Negroes living in these states, approximately eight million (or two thirds of all the Negroes in the United States) reside in the rural districts, the towns and the smaller cities of the South, and it is the problem presented by this group that I shall briefly consider.

In general, it may be said that most of the Negroes of this rural, town and small city group live in communities that are unable to finance adequate control measures as defined by present standards. Unlike their cousins residing in the large cities, they must depend very largely on the state to provide facilities, particularly in the matter of hospitalization. Several of the states listed make no provision whatever for sanatorium treatment for either white or colored patients, and in most of the others the facilities provided are grossly inadequate.

Certainly, the matter of providing an effective service for the control of tuberculosis among Negroes (or, for that matter, white persons) is an extremely complicated one in many of the Southern states, owing to their low economic status. In fact, one may say that there are as yet in existence no adequate data on which to formulate a program that would be reasonably effective and yet within the financial ability of most of these states, and this is particularly evident at the present time.

I shall consider a few of the attempts at meeting this situation.

Tennessee.—The tuberculosis study that is being carried on by the Rockefeller Foundation in Williamson County under the direction of Dr. Bishop has as one of its objectives "the development of a program of control of tuberculosis designated to have practical state-wide application."

A qualitative appraisal of tuberculosis nursing service by officials of the state department of public health gives every indication of materially increasing the efficiency of the service rendered, with no additional cost.

Dr. Overton of the City Health Department of Nashville is experimenting extensively with the use of B C G. It is possible that his results and those of others who are working with this organism will be of value, since B C G, if it can be shown to yield favorable results, is within the financial reach of even the poorest state.

Alabama.—The diagnostic clinic of the Alabama State Board of Health has already standardized on the use of the paper film.

One of the objectives of the study now being made for the Rockefeller Foundation by Dr. Graham in Opelika is to determine "whether or not satisfactory isolation of the tuberculous patient may be achieved at home by the utilization of portable screened cottages and screened porches, together with the provision of adequate public health nursing service, and what it will cost to secure effective isolation by these methods."

Georgia.—Dr. Haygood is now working on a plan for a district tuberculosis nursing service to be operated in conjunction with the state tuberculosis clinic and financed by small contributions from the counties served. The diagnostic clinic of the state health department is trying out the paper film and also planning a change in procedure which, it is hoped, will enable it to examine a much larger number of patients with only a slightly increased expenditure.

It is evident that while the problem of tuberculosis control in the Southern states is a serious one, it is susceptible of at least partial solution. There is reason for encouragement in the fact that this problem is recognized and that attempts are being made to solve it, and also that the Southern states, despite their financial handicaps, have already made notable progress in other phases of public health work.

IS IT ADVISABLE TO USE COLLAPSE THERAPY IN THE TREATMENT OF TUBERCULOSIS IN THE NEGRO?

It may be said that at present the consensus favors collapse therapy as a therapeutic measure, yet a number of clinicians, notably in the Southern states, still believe that it is contraindicated in the Negro.

Dr. Henry D. Chadwick of Detroit will shortly publish an analysis of the favorable results that he has obtained from the administration of pneumothorax to a large number of Negro patients in the several stages of pulmonary tuberculosis. This contribution should add materially to knowledge on this subject.

As to the effect of this division of opinion on control measures, it undoubtedly is a handicap. There seems little doubt, however, that enough definite evidence will soon be accumulated by Dr. Chadwick and others to put it beyond the realm of controversy.

SYPHILIS AND TUBERCULOSIS

From the studies of Wenger, Ricks and others, it would appear that at least 25 per cent of all rural Southern Negroes have syphilis and there is every reason to believe that urban Negroes have at least as high an incidence. It is therefore of the utmost importance to the Negro race that the rôle of syphilis in the high tuberculosis death rate be accurately determined.

There still exist two schools of thought as to the relationship between syphilis and tuberculosis. Some authors maintain that there is an antagonism between these two diseases, and inoculation of the tuberculous patient with the syphilitic virus has been suggested as a therapeutic measure. The weight of opinion, however, is that syphilis reduces the natural resistance against tuberculosis, that it is an important predisposing factor, and that its presence renders the prognosis more grave.

With regard to the treatment of the case in which syphilis and tuberculosis are coexistent, the clinician will gain small comfort either from a survey of the literature or from a consultation with his colleagues, there being only one point on which most of the authorities are in agreement; namely, that the iodides should not be used.

Many clinicians advocate the treatment of syphilis with arsenicals, with no qualification as to dosage. Others believe that while the arsenicals should be used, the dosage should be materially cut down. Still others

are of the opinion that the arsenicals are contraindicated and that bismuth is the medication of choice. Another group of clinicians believe that they obtain better results if the presence of syphilis is disregarded and do not treat it unless it is causing obvious discomfort.

As long as these questions remain unanswered, control measures will obviously be handicapped. In the event that syphilitic soil is shown to favor the implantation of tuberculosis, additional emphasis must be put on the reduction of the present high incidence of syphilis in the Negro, and it is evident that the present variety of ideas as to therapeusis is not conducive to effective treatment. It is not at all unreasonable to suppose that in answer to these questions lies the possibility of an appreciable reduction in the Negro death rate from tuberculosis.

It is interesting to know that Dr. Aronson of Phipps Institute is now investigating this problem.

CONCLUSIONS

1. At present, the control of tuberculosis, particularly in the Negro, is handicapped by lack of exact knowledge regarding several points of importance.

2. Further research is necessary. Studies such as those now in progress at Phipps Institute and in Tennessee, Alabama and elsewhere should add materially to the present limited knowledge regarding the epidemiologic, pathologic and clinical peculiarities of tuberculosis as it affects the Negro and may aid in the solution of some of the administrative problems involved. Regarding the latter, it is suggested that valuable information may be obtained by studying the various adaptations of administrative procedure that various health departments are making to reach more effectively the Negro population.

3. In view of the important sociological aspect of the problem of tuberculosis among Negroes, this line of approach, which appears to have been relatively neglected, should be further developed, perhaps in conjunction with some of the studies now in progress.

450 Seventh Avenue.

ABSTRACT OF DISCUSSION

DR. HORTON R. CASPARIS, Nashville, Tenn.: Dr. Guild brought out that Negro children seem to handle first infections as well as white children. That has been my impression, but Negro adults do badly. The Negro children have nothing to do with their first infections, the Negro adults have everything to do with tuberculosis. There is no specific treatment for tuberculosis and whether or not one gets well depends largely on the individual's more or less sustained cooperation. It would seem, therefore, that the emphasis of control measures should be laid more on prevention. The Negro cannot be depended on to take up that phase of the problem. Reliance must be placed on public health means, official and nonofficial organizations, to go out and find active tuberculosis and to eliminate it as a source of infection. Infected children must be helped either with BCG, if that proves satisfactory, or with other means.

DR. MARIE PICHEL LEVINSON, New York: I cannot refrain from adding a word about a measure that I consider preventive. In New York there is a contraceptive clinic for Negroes. I believe it is the first one in the country. A branch is located in Harlem, which is the district in New York having the greatest death rate from tuberculosis. It was felt that in this neighborhood particularly where the infant mortality was so great a proper response from the Negro population was not being obtained. After three years' existence it was found that more white patients than Negroes were coming to the Negro clinic, so last month the headquarters were moved into the New York Urban League Building, which is a settlement house for the advancement of everything relating to Negroes, and the number of Negroes coming to the clinic for such advice has increased. I feel that this is a very necessary public health measure and I believe it is an adjunct to attacking the problem preventing tuberculosis. New York City has a large Negro problem and we are just as concerned there as people are in the South. The various social agencies refer tuberculous or pretuberculous women to our clinic for contraceptive advice as a preventive measure.

DR. EMIL BOGEN, Olive View, Calif.: I have been interested in trying to find why certain races show a higher mortality rate from tuberculosis. I have tried to find out by animal experimentation what will make one strain or family of animals more susceptible to tuberculosis than another. Larger doses of infection will with fair uniformity produce larger amounts of tuberculosis. I have not been able to find any difference by environmental means affecting the development of tuberculosis in animals after they have been infected. I think one has to distinguish, when speaking of environment, between those environmental factors affecting exposure to infection, or the number of germs that the individual receives, and those factors affecting his resistance to the infection. Certainly it can be shown, both by animal experimentation and by epidemiologic studies, that tuberculosis depends greatly on the number of organisms. Cases can be traced from one active case to another. It is much more difficult to show that such things as income or housing conditions or food really affect the development of tuberculosis in different peoples. It is also known that, after tuberculosis develops, the course of the disease depends very much on the treatment and that at the institution with which I am connected we find that the Negroes or those of any other race coming in with early tuberculosis have a very good chance of recovering. I feel that one of the greatest factors responsible for the different mortality rates in different races is the readiness with which the different people come for early treatment.

PROGRESSIVE PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY

RESULTS OF TREATMENT WITH EPINEPHRINE AND PILOCARPINE

GARRY DE N. HOUGH, JR., M.D.
SPRINGFIELD, MASS.

For nearly a century this poorly understood symptom complex has been recognized and has presented a constant challenge to the medical profession. The various therapeutic procedures recommended, including exercises, physical therapy, dietary regulation, calcium and glandular preparations, have all failed to have any appreciable influence in improving the condition or in stopping the gradual relentless progression to complete helplessness.

In 1930, Kuré and Okinaka [1] reported improvement in nine cases following the daily administration of epinephrine and pilocarpine. In 1931, I [2] reported improvement in sixteen cases in which this treatment was used. This paper is based on the present results in these and twenty-two additional cases treated over the period of the last three years at the Shriners Hospital for Crippled Children at Springfield, Mass.

In addition to my own cases I have collected results in fifty-six cases in which this treatment was given

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1. Kuré, K., and Okinaka, S.: Behandlung der Dystrophia musculorum progressiva durch kombinierte Injektionen von Adrenalin und Pilokarpin, Klin. Wchnschr. **9**:1168 (June 21) 1930.
2. Hough, G. deN., Jr.: Progressive Pseudohypertrophic Muscular Dystrophy, J. Bone & Joint Surg. **13**:825 (Oct.) 1931.

elsewhere, thirty-one being from the literature [3] and twenty-five from personal communications. According to the various observers, improvement has been noted in thirty-nine, fifteen have been unchanged, while in two the condition has become worse under treatment.

I have used epinephrine-pilocarpine in thirty-eight cases in all stages of the disease, the number of injections varying from twenty-three to over 600. Administration has been by daily hypodermic injections of 0.3 cc. of a sterile solution consisting of one part of 1 per cent solution of pilocarpine hydrochloride and two parts of 0.1 per cent (1:1,000) epinephrine hydrochloride. The drugs have no incompatibility and may be dispensed together in a rubber capped vaccine bottle and the daily dose removed under aseptic precautions.

Every patient has shown some clinical improvement while taking the treatment. This improvement has been both subjective and objective. It has varied in amount from a slight sense of increased strength with a greater desire to attempt functional activity to apparently complete recovery. In most cases some definite functional improvement could be demonstrated. The improvement was greatest in the least advanced cases.

There have been no additional therapeutic procedures other than general hygienic care, ordinary diet, and normal activity to the limit of the individual capacity. In particular, glycocoll has not been used in spite of some encouraging reports, because of my desire to evaluate as accurately as possible the influence of pilocarpine-epinephrine.

It is obviously impossible to eliminate the psychologic factor of a definite course of treatment, particularly in cases in which previously repeatedly hopeless prognoses have been given. The hopefulness and optimistic attitude of the parents very probably has been reflected in the mental condition of the child, and due allowance for this factor must be made. This is particularly true when the improvement has been primarily subjective or when it has been relatively slight.

Fifteen cases have been observed for from one to two years since the last treatment was given, from sixty-nine to 240 injections having been given. In only one case is there any evidence that the progress of the disease has been stopped. The patient, a 13 year old boy with symptoms for eleven years, had been confined to a wheel chair for three years. He has apparently not changed during the past year following 240 treatments. Every other case has shown definite progression of the disease, in spite of 200 treatments in one case, 180 in another, and from seventy to ninety in the remainder.

Nineteen patients are still receiving treatment, nine of whom have been under treatment too short a time to present evidence on the question of progress, having received less than 150 injections. Ten patients have received from 150 to 600 injections. Four of these children have shown some loss although still as well as, or better than, when the treatment was started. The other six patients have maintained their improvement.

From this evidence I have arrived at the definite conclusion that, although epinephrine-pilocarpine is helpful and of symptomatic benefit, it is not curative.

The treatment must be continued indefinitely and even in spite of continued treatment the condition may progress.

I have attempted to determine the influence of the treatment on the duration of life by an analysis of fifteen fatal cases, ten from my own cases and five from the literature.[4] As shown in the accompanying table, the four treated cases show a somewhat greater variation of age at time of death, and the average age is about a half year older than in the treated cases. While this suggests a possible lengthening of life, there is not sufficient difference to be of significance.

The remaining problem to be answered is whether this treatment prolongs the period of functional activity. An analysis of ninety-five cases, eighteen of which have been taken from the literature, shows that symptoms are first observed before the age of 2 years in about 12.5 per cent of the cases, from 2 to 4 in 50 per cent, and from 5 to 7 in 30 per cent. In only an occasional case were symptoms first noted after 7 years.

Fatal Cases

Name	Age	Cause of Death	Duration of Disease	Years Unable to Walk
Treated:				
D. R.	9	Acidosis	4	2
Case 5	16	Acute appendicitis	11	5
Case 10	16	Pneumonia	14	7
Case 1	20	Pneumonia	12	7
Average	15.3		10.3	5.3
Untreated:				
W. D. (Voshell)	12	Bronchial disease	..	..
Bishop (1) (Voshell)	12	Whooping cough	..	4
Bishop (2) (Voshell)	12	Stomach trouble	..	4
Case 2	13	Pneumonia	10	3
Case 13	15	Pneumonia	8	1
J. D. (Voshell)	15	Unknown	..	..
Case 6	16	Unknown	10	3
Case 16	16	Influenza and tuberculosis	15	6
W. P. (Voshell)	17	Unknown	..	..
Case 15	17	Gastro-enteritis	15	7
Case 17	17	Pneumonia	16	8
Average	14.7		12.3	4.5

In a few cases the power of locomotion is lost as early as two years after onset, and 35 per cent of the children are unable to walk after 5 years. Most of the remainder (62 per cent) lose their ability to get about between the sixth and the ninth year of the disease. In only an occasional case is gait preserved beyond nine years. Expressed in terms of the child's age, approximately 50 per cent stop walking at the age of 8 to 9 years and 40 per cent at from 10 to 12 years.

The treatment has been carried out in twelve ambulatory and twenty-four nonambulatory cases. In the latter group, in spite of the fact that in every case some improvement was observed, in no case was gait reestablished. Two of the twelve ambulatory patients have since lost the power to walk, at an age of 11 years, after seven and eight years of the disease. Both of these children show a possibly suggestive but probably insignificant increase over the average. The patients who are still ambulatory vary in age from 6 to 13 and average 9.2 years, which is slightly beyond the age at which most of the children lose their power to walk.

CONCLUSIONS

I feel justified in making the following conclusions regarding the use of epinephrine and pilocarpine in progressive pseudohypertrophic muscular dystrophy:

1. Daily doses of 0.1 cc. of 1 per cent solution of pilocarpine and 0.2 cc. of 0.1 per cent epinephrine are of symptomatic benefit in practically all cases.

3. Kuré and Okinaka (footnote 1). Voshell, A. F.: Progressive Pseudohypertrophic Muscular Dystrophy, South. M. J. **26**: 156 (Feb.) 1933. Goralewski, G., and Engel, E.: Zur Behandlung der Dystrophia musculorum progressiva mit Adrenalin und Pilokarpin, Deutsche med. Wchnschr. **58**: 1169-1170 (July 22) 1932. Leiter, A.: Die Adrenalinbehandlung bei progressiver Muskeldystrophie, Monatschr. f. Psychiat. u. Neurol. **81**: 289 (Jan.) 1932.

4. Voshell (footnote 3).

2. In some of the cases the improvement may be wholly or in part due to the psychologic effect of renewed hope based on a definite course of treatment.

3. This improvement has never been sufficient to reestablish gait after the power to walk was lost, but function when present may be markedly improved.

4. There is no evidence that this treatment is curative or that it alters the mortality or increases the length of life.

5. If treatment is stopped for a period of from one to two years, the gradual increase of disability is again noted.

6. Progression may occur while under treatment, but apparently the rate of progress is definitely slower than it otherwise would be.

7. It is possible that alteration of dosage or the combined use of other methods of therapy may give better results.

8. Finally, in spite of the fact that these drugs do not cure the disease, that their benefit is not permanent or as marked as the early reports may have led one to hope, epinephrine-pilocarpine treatment is of sufficient value to justify its continued use in this disease. There is no more excuse for withholding it than there is for not giving insulin in severe diabetes or digitalis to an individual with irreparable cardiac damage. Even these highly valuable therapeutic agents are not curative.

146 Chestnut Street.

ABSTRACT OF DISCUSSION

DR. ARTHUR STEINDLER, Iowa City: The interpretation of this condition from the pathologic and etiologic points of view will have to abide its proper time. I believe it was Duchenne de Boulogne who pointed out that this condition is a disease of the muscles and not of the central nervous system and that consequently all methods of treatment that were directed to the central nervous system would come to naught. So, when in 1929, Kuré and Okinaka came out with their pilocarpine-epinephrine method there was some raising of eyebrows. They, were able, however, to present a series of twelve cases, six of which improved and two were cured. Dr. Hough today presents a series of thirty-eight cases in almost all of which at least temporary improvement was noted. The question of glycine, or glycocoll, treatment ought to be given consideration. When Powers and Techner brought out their chemical investigation on this subject, they pointed out that the creatine was utilized to the degree of 70 to 80 per cent. Others, Gibson and Martin and Brand, demonstrated the synthetic power of the organism to utilize creatine. Gibson and Martin accomplished this by feeding gelatin and Brand by feeding glycine, or glycocoll. Clinical reports on the use of glycine, or glycocoll, above all, the reports of Milhorat and his co-workers describe a certain amount of temporary improvement. The basic idea being that the glycine furnishes the food for the muscles which would otherwise be lost by excessive excretion of creatine, it is believed that the treatment should be employed only in those cases in which the initial excess of creatine excretion in the urine and in the muscle tissue disappears after one week of creatine dosage. Voshell reports fourteen cases; nine were improved and five were not improved. His idea was to combine the pilocarpine-epinephrine with the glycocoll treatment, assuming that the glycocoll would furnish the food for muscles that would otherwise be lost, whereas the epinephrine would provide the stimulation of the autonomic system necessary for the control of creatine metabolism. It is obvious that those cases in which creatine metabolism has been hopelessly upset and is continually affected by an excessive creatine output would not be suitable. I have recently reviewed my own cases, eighty-one in number. Not in a single case was I able to effect an arrest of the condition, although all possible methods have been used, including epinephrine and glycine.

DR. HENRY B. THOMAS, Chicago: At the University of Illinois College of Medicine, cases of dystrophy have been admitted for study since 1931. We have in only a few cases, used epinephrine and anterior pituitary, with no noted improvement. We have used glycine with no clinical improvement; also creatine. I believe that any therapy after function is lost will be of no avail. The etiology of the disease must be sought in order that the loss of muscular function may be prevented. We are anxious, therefore, to experiment on the metabolism of these patients and have our plans laid to proceed along this line. In most cases the diagnosis, as Dr. Hough says, is easy. However, caution is urged in order to prevent mistakes in diagnosis in obscure cases. We have one case in which there is a coexistence of infantile and muscular dystrophy. We have also one case which we have been calling amyotonia for some time. Closer examination proved it to be an instance of muscular dystrophy of the atrophic form. When 8 months old, the patient contracted scarlet fever. After that his muscles grew gradually weaker and he became more deformed. This case, and the one I mentioned before, show a connection with an acute infectious disease. Out of our 634 hospitalized orthopedic cases since 1931, we have included and studied eighteen instances of dystrophy, or about 2.75 per cent of our admissions. The pseudohypertrophic form of the disease was presented by 38% per cent, all boys. The ages ranged from 3 to 14. There were thirteen boys and five girls. That is a proportion of 2.6 to 1. Two are brother and sister, and the third a maternal cousin. One patient has a sister with a similar condition. Thus in four instances the disturbance was of the familial type. In four of the patients an intercurrent disease, such as pneumonia or whooping cough, proved to aggravate the already existent muscular dystrophy, and two-thirds per cent have never walked. Fifty per cent walked normally until the age of 3 to 20 years, and then motion became gradually impaired. At the present time 22⅔ per cent of them are unable to walk; the remainder have difficulty in walking, especially in climbing up and down stairs. Weakness of the legs since birth was present in 33⅓ per cent. The mental development of these patients has been normal. Well pronounced pseudocontractures were found in 44⅘ per cent. The muscles of the thigh, knee and ankle were usually involved.

DR. PHILIP LEWIN, Chicago: I want to express my appreciation of the work that Dr. Hough has done on this subject. I began using epinephrine in 1920. In order not to have to make punctures three times a day, I administered hypodermic tablets of 1/300 grain dissolved under the tongue, which seemed to me a better way than ingestion by mouth, which proved to be worthless. There seems to be an analogy in this condition such as exists between the situations of a coal bin, a furnace and a fireman. The fuel may be deficient in quality, quantity or availability. The furnace may be inefficient. The fireman may not have proper ability, strength or industry. The transportation may be wrong so far as speed, direct route, obtainability or detours are concerned. The energy may be at fault so far as quantity, availability and usability are concerned. So far as muscles are concerned, the three factors are the efficiency, the ability to store up fuel and the ability to transform the fuel.

When Kuré and Okinaka in 1930 reported two cures and seven improved cases, I thought that it was an addition to the armamentarium; but I don't think that Dr. Hough's series, Dr. Voshell's series, or any other series I have studied proves that point. There is undoubtedly something in it. The question seems to revolve about the metabolism. Until the metabolism is thoroughly understood, any method is going to be a hit-or-miss method. There are other forms of treatment, such as glycine, pituitary extract, diet, combinations of the Japanese and glycine treatments, and blood transfusions. I should like to try the method of giving fetal muscle extract. Milhorat, Techner and Thomas are using from 5 to 15 Gm. of glycine a day, increasing the output of creatine, but it must be continued indefinitely. I think the word "improved" is misleading, because any change from a poor routine may be beneficial. The children that are seen for the first time have been under a poor routine, and any change may help them. It must be considered that the course of the disease may have remissions and these may be attributed to the therapy.

DR. GARRY DE N. HOUGH, JR., Springfield, Mass.: Of course, this is simply one phase of a complicated subject. I agree that there is a tremendous amount of information to be learned in order to come anywhere near understanding this disease, and I think that eventually this condition will be subdivided into types and groups, probably as distinct entities. What is now classified as progressive pseudohypertrophic muscular dystrophy may represent a number of different conditions. I am convinced that epinephrine and pilocarpine are beneficial although not curative. Dr. Lewin criticizes the use of the word "improved." In many of the cases perhaps the change has not been sufficient to warrant the use of this term, but my most satisfactory patient, after being under observation for five years, last summer passed his test as a life saver and won a quarter-mile swimming race. If, after five years of disease, he was able to do that, I think he was improved. He is classified, however, as having shown progress, because for three years he represented a complete cure, walking with normal gait and taking part in all normal activities. Now he has a definite limp, walking with a side-to-side sway.

Clinical Notes, Suggestions and New Instruments

CARCINOMA OF BARTHOLIN'S GLAND

REPORT OF TWO CASES

HYMAN STRAUSS, M.D., BROOKLYN

Primary carcinoma of Bartholin's gland is rare. A review of the world's literature by Harer in 1933 revealed only thirty cases recorded, not all of which in his opinion were authenticated. Nothing definite is known about the etiology. Falls says that chronic inflammation has been present in a considerable number of the cases reported. In only one case was there a definite history of gonorrhea and syphilis. Bilateral inflammation of the gland was described in only one case. The lesion has been found in unmarried women but not in virgins. The youngest patient was 28 and the oldest 91, while the average age was over 50 years.

Diagnosis is usually made postoperatively. It is most frequently confused when associated with chronic infection with abscess formation. Syphilis, contrary to gonorrhea, rarely attacks this gland. Chancroid and granuloma inguinale affecting Bartholin's gland have not been reported. Primary tuberculosis is rare, there being only three cases reported. Viet found reports of three cases of sarcoma of this gland. The prognosis, according to Kelly, is usually fatal because of late discovery or incomplete operation. In the cases reported, one patient survived for three and another for six years free from recurrence. Metastasis occurs in the inguinal lymph glands quite early.

The treatment is primarily surgical. However, at Radiumhemmet, in Stockholm, electrocoagulation of the tumor and radiotherapy have been used with considerable success. Howard Kelly advises endothermic vulvectomy and electrocoagulation of the glands in situ. Taussig, who has made a study over a period of years, insists that radical vulvectomy and a complete bilateral Basset operation is the only procedure that has stood the test of time. If the lesion is early or the risk slight, he performs this operation in one stage; otherwise it is done in two stages with an interval of a few weeks. He has not been satisfied merely with excision of the vulva and irradiation of the regional lymph nodes.

REPORT OF CASES

CASE 1.—Mrs. C. M., aged 61, white, an American, was admitted to the gynecologic clinic of the Brooklyn Cancer Institute, Jan. 15, 1932, with swelling of the right side of the vulva, which had been noticed for a few months. At first the swelling was small, firm and painless. In spite of hot compresses and other remedies applied to the lesion, it increased in size. She was referred to the clinic by her physician. There was nothing of interest in her previous history. She was a tertigravida and a tertipara. The menopause occurred at 54. During the year before admittance, the patient had frequent spells of hemoptysis.

On admittance the patient was emaciated, weighing 74 pounds (33.6 Kg.). Examination of the genitalia showed a mass measuring 8 by 4 by 3 cm., involving the right labium majus and almost occluding the introitus. The tumefaction was firm, smooth, not tender, and with no area of fluctuation. The mass was not fixed to the underlying tissues but was adherent to the overlying skin, which was reddened. The inguinal nodes were not appreciably enlarged. Otherwise the genital organs presented no abnormalities. The Wassermann test was negative and the sputum was repeatedly negative for tubercle bacilli.

Examination of the blood revealed: red blood corpuscles, 3,080,000, with no early forms; hemoglobin, 90 per cent; white blood corpuscles, 18,200; polymorphonuclears, 84 per cent; lymphocytes, 11 per cent; monocytes, 4 per cent; eosinophils, 1 per cent.

A roentgenogram of the chest showed no cavities or consolidation, but veiling over both apical fields, an evidence of a thickened pleura. The lung root densities were not abnormal in size. There was some calcium deposit.

A diagnosis of carcinoma of Bartholin's gland was made and operation was performed January 28. The involved area was completely excised. The pathologic diagnosis was anaplastic carcinoma of Bartholin's gland.

Interstitial radium therapy was administered to the right labium at the site of the incision, March 9. Two tubes of 9 mc. each of radon filtered through 0.5 mm. of platinum were inserted and allowed to remain in place until a dose of 1,200 millicurie hours was delivered. In May, a course of high voltage roentgen therapy was administered to the pelvis and perineum, five portals being used. A total of 6,450 roentgens was administered over a period of twenty-one days.

The patient was seen in the follow-up clinic from time to time. In January, 1933, a small erosion was noted at the site of the operative scar. Further radiation was prescribed. This was given by applying two gold filtered radon seeds of 1 mc. content each, delivering a total dosage of 266 mc. hours. Since then the lesion has remained completely healed.

CASE 2.—Mrs. M. L., aged 48, white, American, admitted, Feb. 16, 1933, to the gynecologic service of Kings County Hospital, service of Dr. H. M. Mills, complained of a lump in the vagina and a vaginal discharge. Two years prior to admission, the patient noted a small mass slowly increasing in size. Four months before admission, the mass grew rapidly and a whitish to bloody vaginal discharge occurred. One month before admission, bleeding from the lesion and vaginal pain radiating to the right thigh set in.

The pain was sharp and stabbing. She lost 5 pounds (2.3 Kg.) in two months. She was a primigravida in 1909 and there was a miscarriage, after which complications developed necessitating a hysterectomy. In 1929 the patient had a cholecystostomy, which was later followed by a cholecystectomy.

The patient was obese and did not appear acutely ill. Rectal examination was negative. The right labium majus was enlarged by a mass about the size of a walnut, which protruded over the introitus and practically occluded the vagina but did not extend to the inguinal or perianal areas. It was irregular in outline, much indurated and exquisitely tender. The overlying skin was adherent, swollen, reddened, edematous and beginning to ulcerate. The mass was slightly fixed to the underlying tissues. There was an ulcerated area about 25 mm. in diameter at the exit of the duct, which extended three-fourths inch along the vaginal wall. This area bled readily. The vagina otherwise appeared normal. The uterus presented no pathologic changes; the adnexa were not palpable. A brownish discharge was present. The inguinal lymph glands were not palpable. Roentgen examination of the chest revealed no pathologic changes.

The blood Wassermann reaction was negative. Chemical examination of the blood revealed sugar, 114 mg. per hundred cubic centimeters; creatinine, 1.25; urea, 35. The blood count revealed: red blood corpuscles, 4,192,000, no early forms; hemoglobin, 85 per cent; white blood corpuscles, 5,200; poly-

From the Department of Gynecology, Kings County Hospital, Dr. H. M. Mills, Director, and the Department of Radiology, Division of Cancer, Dr. I. I. Kaplan, Director.

morphonuclears, 61 per cent; lymphocytes, 36 per cent; large mononuclears, 3 per cent.

Examination of a catheterized specimen of urine revealed a specific gravity of 1.021; acid; no sugar; a trace of albumin; many fine granular casts, many leukocytes; an occasional red blood corpuscle.

A diagnosis of carcinoma of Bartholin's gland having been made, a radical vulvectomy was done, February 24. The wound healed slowly because of secondary infection. Six weeks after the vulval wound had healed, a bilateral Bassett dissection of the inguinal and femoral glands was done. The pathologic diagnosis made by Dr. Hala was squamous cell carcinoma, but there was no evidence of metastasis in the lymph glands removed. The convalescence was uneventful. The patient when last seen, June 30, 1933, was free from symptoms and there was no evidence of recurrence.

755 Ocean Avenue.

A PATIENT SENSITIZED TO AN ART GUM ERASER

JUNE ADKINSON, A.M., AND I. CHANDLER WALKER, M.D., BOSTON

Although this case is not of widespread interest to the community at large, it does concern those who use extensively art gum erasers, such as artists, art students, architects and masseurs.

A woman, aged 25, normal with the exception of a defect of vision which is corrected by wearing glasses, daily used a binocular microscope for from one to five hours a day without eyestrain. Recently she began to draw from the microscopic field for several hours at night and often for all day on Sunday.

After a short time the patient noticed a persistent itching of the eyes and edema of the eyelids, which could be relieved temporarily by rubbing the eyes with her hands. Later on, even when she did not touch the drawing materials for several days, the swelling and redness of the eyelids would persist and there was a marked increase of the symptoms whenever the drawing was resumed. Still later there was constant redness, rawness and itching at the corners of the mouth and the usual symptoms of a slight cold. A marked rhinitis and a sensation of soreness in the throat occurred whenever the patient was exposed to the drawing materials. This condition continued for seven weeks.

Fearing that the additional strain on the eyes from the prolonged periods of drawing was injuring her sight, the patient consulted an ophthalmologist, who found that her vision was unchanged, in spite of the excessive use of the eyes. From the history and the appearance of the eyelids and the corners of the mouth, the ophthalmologist felt that the condition was allergic in nature and was caused by some substance to which she was only recently exposed. Skin tests were advised with toilet preparations, drawing materials and other substances such as clothing and gloves.

Since her toilet preparations were of the same brand that she had used for years and since the only change in her environment and occupation was the drawing and furthermore because the symptoms, which started soon after she began to draw, were aggravated whenever she used the drawing materials for a long time and were relieved when she was not exposed to them, the patient thought that the paper, the ordinary rubber eraser, the soft viscous art gum eraser or a cement used for mounting pictures was probably the offending factor.

The drawing materials were avoided for several days until the eyelids were only a little swollen and there was very slight itching. When the patient was nearly normal again, skin tests by the scratch method were made on the left forearm with toilet preparations, with rubber eraser, soft art gum eraser, picture mounting cement and drawing paper. A very small amount or piece of each substance was placed on a slight cut made with a sharp scalpel, penetrating the cuticle but not drawing blood. A drop of tenth-normal sodium hydroxide was placed on each scratch to dissolve the fragment of material and allowed to soak for fifteen minutes, after which the scratches were gently wiped off and the reactions were compared with a control scratch on which only a drop of tenth-normal sodium hydroxide had been placed. The tests with the toilet preparations were entirely negative, the tests with the rubber eraser and the drawing paper were slightly red, but the test with the art gum eraser produced an urticarial wheal 0.75 cm. in diameter surrounded by a flushed area about 2 cm. in diameter.

Although the eyelids were only slightly itching and swollen before the skin tests were made, on the following morning and apparently as a result of the skin tests, both eyelids were badly swollen and the itching was severe. The swelling disappeared rapidly and the patient was fairly comfortable for several days or until the following Sunday, when she spent several hours drawing with the same materials. After this exposure the swelling and itching of the eyes reappeared and continued for about twenty-four hours. The corners of the mouth were not affected after the tests or after this prolonged exposure to the drawing materials, probably because the patient, who had had the habit of holding her pencil, contaminated of course with eraser and paper dust, in her mouth while erasing, was very careful to avoid touching her face with her hands and the drawing materials. During the five days of avoidance of drawing, the eyelids became almost normal.

On the fifth day after the last exposure, a more extensive series of scratch tests was made on the other forearm with foods, pollens, animal hairs and feathers, all of which gave entirely negative reactions. In addition, retests were made with solutions of the drawing materials. The solution of rubber eraser gave a negative reaction, the solutions of cement and of drawing paper gave a slight erythema, but the solution of art gum eraser gave a definite itching raised area about 1 cm. in diameter surrounded by a flush about 3 cm. in diameter.

About two hours after the second series of tests was made, the left cheek began to redden and burn, and an hour later, about 5 o'clock, a definite urticarial wheal appeared on the left cheek. By 8 o'clock there was itching and marked swelling of both eyelids as severe as the symptoms produced by several hours' use of the drawing materials to which the patient had not been exposed for five days. Application of fresh menthol ointment gave sufficient relief for her to go to sleep normally.

About 2 o'clock in the morning the patient was awakened by a very severe burning sensation in both eyes. The eyelids were so edematous that the left eye could hardly be forced open. The lips were stiff, swollen, protruding and hot, and there was a severe rhinitis. The throat was not affected, but the patient was frightened and in mental distress. The application of boric acid solution gave no relief, but acetylsalicylic acid tablets and the application of fresh menthol ointment relieved the symptoms in a short time. On the following morning, although the edema was somewhat reduced and the itching had subsided, the eyelids were still badly swollen and two or three hivelike areas appeared on the cheek and neck. After the application of menthol ointment at 11 o'clock, the facial swelling receded rapidly.

Examination of the test area on the arm showed that all scratches were normal where the tests had been negative on the previous day. The scratches to which the solutions of picture mounting cement and rubber eraser had been applied were negative and the scratch on which a solution of drawing paper was tested showed a slight redness; but the scratch on which the art gum eraser solution had been placed showed redness and erosion about 0.75 cm. in diameter.

In order that the drawing, which was an unaccustomed occupation, might be finished, a plan was made for the patient to protect herself from exposure to the dust of art gum eraser and drawing paper dust by smearing her face heavily with ointment of rose water, by wearing a damp gauze mask over her mouth and nose, and by protecting her eyes with glasses. With these precautions, the patient was able to continue her drawing for two and one-half hours on one day, five hours on another and longer periods with no return of the itching and edema. Any use of the art gum for erasing without the facial mask caused a beginning of the itching and swelling of the eyelids, but erasing done with the ordinary rubber eraser produced no discomfort even without the mask.

A slight return of the irritation of the eyelids was noticed whenever the patient sat in the room where the drawings had been made. After a thorough dusting of the furniture and of the work table with a damp cloth, and beating of the rug outdoors, the patient experienced no further trouble in the room.

From the Medical Clinic of the Peter Bent Brigham Hospital.

Still later, when the patient visited the store where the art gum was purchased, she stood near a counter on which were exposed brick-shaped large pieces of the art gum material to be used on their hands by masseurs in rubbing patients for weight reduction. The odor or dust of the material was so abundant that the patient felt an immediate effect in her eyes and throat and she retired for relief to the sidewalk until her purchases were ready.

721 Huntington Avenue.

Council on Pharmacy and Chemistry

PYRIDIUM OMITTED FROM N. N. R.

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. PAUL NICHOLAS LEECH, Secretary.

Pyridium[1] is the monohydrochloride of an azo dye of the pyridine series, phenylazo-*a*-*a*-diamino pyridine. It is marketed by Merck & Co., Inc., in the form of a 1 per cent aqueous solution, a 10 per cent ointment, and tablets containing 0.1 Gm. The firm presented the product for consideration of the Council in 1928, proposing it for use mainly as a urinary antiseptic. The A. M. A. Chemical Laboratory examined the product and evaluated suitable standards of stability and purity, as well as corroborating the claimed composition.[2]

The firm's original presentation of Pyridium was accompanied by four circulars containing claims and excerpts from a pamphlet by Iwan I. Ostromislensky, entitled "The Scientific Basis of Chemotherapy." Ostromislensky, who originated Pyridium in 1912, appears to have used the drug first in Russia in 1917 and brought it with him to this country for clinical trials and manufacture about 1924; the base apparently was first described by Tschitchibabin and Zeide. Most of Ostromislensky's book on chemotherapy is concerned with an account of Pyridium. This evidence was judged to be unconvincing. The Council declared Pyridium unacceptable in July, 1928, and adopted for publication a statement of its consideration. A request by Merck & Co., Inc., for postponement of publication of this report was granted.

Additional evidence was presented by the firm in April, 1929, and further postponement granted. A recommendation to accept Pyridium in December, 1929, was not adopted because it was desired to obtain opinions on the evidence from critical genito-urinary surgeons. In March, 1930, opinions on the value of the evidence for Pyridium were expressed for the benefit of the Council by two prominent genito-urinary surgeons, consultants of the Council, who considered the evidence submitted to be insufficient to support the claims but did not advise rejection of the product. Further postponement of action by the Council was decided on.

While these negotiations with the Council were being carried on by Merck and Co., the Mallinckrodt Chemical Works began to push the sale of Mallophene and E. R. Squibb and Sons began to exploit Serenium; Mallophene (for which the firm has indicated willingness to substitute the nonproprietary name Azophene) is identical with Pyridium, as shown by an investigation in the A. M. A. Chemical Laboratory, while Serenium is an azo dye of a similar type. The firms of Mallinckrodt and Squibb did not submit their products to the Council at that time, and Merck and Co. appeared to be suffering a loss through its attempt to cooperate with the Council. A recommendation that Pyridium be accepted for one year was adopted in April, 1930. The referee stated in the discussion of this action that both genito-urinary consultants favored acceptance. After discussion of the evidence, the Council announced acceptance of the product.[3]

Pyridium was retained in New and Nonofficial Remedies during 1931. On the basis of new evidence presented by the firm, the Council's referee, in May of that year, obtained an opinion from one of the consultants that Pyridium still gave promise of therapeutic usefulness, but the other consultant was not convinced by the new evidence. This evidence was chiefly voluminous unpublished reports submitted by the firm. The Council voted to accept Pyridium for another one-year period, although at the time a member of the Council stated that he feared that in a few years pyridium will join the ranks of discarded urinary antiseptics.

A new referee was then assigned the task of reviewing the old and new evidence on Pyridium. He recommended reacceptance of Pyridium under severely limited claims, and in November, 1931, the Council adopted this recommendation. The conditions specified for this reacceptance considerably restricted the claims for Pyridium. The restrictions were, in brief, that the firm should not emphasize the tissue-penetrating property of Pyridium, should limit claims for efficacy of the drug in the treatment of prostatitis and pyelitis, should omit all claims that the drug protects the tissue cells against bacterial toxins and stimulates body defense, regeneration and repair of tissues, and should refer explicitly to possible gastro-intestinal disturbances sometimes produced by the drug. The firm agreed to abide by these requirements and in later correspondence with the referee, through the Secretary, agreed to drop its claim that Pyridium taken by mouth gives a bactericidal power to the urine. An antibacterial or bacteriostatic action of urine containing excreted Pyridium seemed to have been established according to the evidence reviewed at that time.

During 1929, bacteriologic reports had been received from the Lederle Laboratories, the Pease Laboratories, the Gradwohl Laboratories, and Professor Prescott of the Massachusetts Institute of Technology. All of these indicated that Pyridium in various solutions had bactericidal and bacteriostatic effects on B. coli and Staphylococcus aureus. They favorably impressed the previous referee. They are in harmony with other similar laboratory examinations considered by the Council. They lacked data on the antiseptic property of urine containing excreted Pyridium, and clinical reports also were lacking.

Finally, the firm has stated that it has numerous letters from physicians testifying to the efficiency of Pyridium. These have not been submitted. They could not be considered as having any definite value as evidence. The firm sent a reference to a report on Pyridium by Szancer in the *Pharmazeutische Nachrichten*, Warschau, 1930, Przemysl. This journal not being available to the referee, he has not examined the report. Other expressions of opinion unfavorable to Pyridium have been made by Dr. Keyes[4] and in the Queries and Minor Notes section of THE JOURNAL.[5]

In July, 1932, Merck & Co., Inc., submitted the text of a proposed advertisement of Pyridium as a "first aid" antiseptic, indicating its intention to exploit the product to the public as an "effective" antiseptic for local use on cuts, wounds and abrasions. The referee replied through the Secretary that he did not have sufficient evidence to justify acceptance of Pyridium for these purposes and asked the firm to submit the evidence before proceeding on this plan of exploitation. The firm decided to abandon this plan.

A review of the firm's advertising convinced the Council's referee that it has been restrained within the specifications of the Council as far as the use of words is concerned. The referee believes that Merck & Co., Inc., has made a faithful and expensive effort to comply with the regulations of the Council.

The Council's referee presented the following summary and the conclusions which he has drawn from his consideration of the reports on Pyridium. An annotated list of the papers and reports studied by the referee (except where otherwise noted) appears as the first addendum to this report.

1. Azophene (formerly Mallophene), marketed by the Mallinckrodt Chemical Works, is identical with Pyridium. The Council's report rejecting Azophene appears in this issue of THE JOURNAL. A somewhat similar product, Niazo, also recommended for use as a urinary antiseptic, is marketed by the Schering Corporation. The Council's report rejecting this product appeared in THE JOURNAL, June 3, 1933, p. 1767. Serenium does not stand accepted.

2. Collins, G. W.: Chemical Examination of "Pyridium" and "Mallophene," J. Am. Pharm. A. **20**: 455, 1931.

3. Pyridium, J. A. M. A. **95**: 34 (July 5) 1930.

1. Pyridium in aqueous solution has bactericidal and bacteriostatic properties. These effects are less against B. coli than on Staphylococcus aureus. These effects are reduced by urine and liquids containing complex organic substances.

4. Keyes: Urology, 1928, p. 111.

5. Pyelitis After Otitis Media, J. A. M. A. **99**: 584 (Aug. 13) 1932.

2. Urine secreted after oral administration of Pyridium has no bactericidal effect on B. coli and a negligible bacteriostatic action. Occasionally, urine containing excreted Pyridium may be bactericidal and bacteriostatic against Staphylococcus aureus. The lack of these effects may be due to inability practically to obtain a sufficiently high concentration of the substance in the secreted urine or to a change in the substance in its passage through the body. Since Pyridium does not cause the secretion of an antiseptic urine, it cannot be sustained as a urinary antiseptic.

3. Numerous clinical reports on Pyridium therapy in infections of the urinary tract are open to doubt and do not present convincing evidence. Evidence denying its efficacy is accumulating in published reports and in less formal expressions of competent urologists. During eight years of trial, Pyridium has not become established as a useful remedy.

4. The earlier claims that the drug detoxified bacterial poisons, aided the defenses of the body, and stimulated tissue repair have not been supported and have been withdrawn.

5. No convincing evidence has been presented that Pyridium is a useful antiseptic for application to infected wounds, either in treatment or as a prophylactic.

6. Penetration of tissues, especially mucous membranes, has been demonstrated. But there is no experimental or clinical proof that the amount and character of the compound in the tissues and mucous membranes are such as to kill bacteria or hinder their growth.

The Council's referee recommended, therefore, that the acceptance of Pyridium be revoked at once and that the product be declared unacceptable for continued inclusion in New and Nonofficial Remedies as a local, general or urinary antiseptic because claims for its therapeutic usefulness are not warranted by the accumulated evidence. The Council adopted the referee's report and authorized publication of this statement of the Council's consideration of Pyridium.

When the foregoing report was submitted to Merck & Co., Inc., the firm replied in a carefully prepared and well documented brief which required further consideration by the Council. The thesis of the firm's brief was that Pyridium has become established as a useful remedy. To uphold this, the firm offered (*a*) informal reports from physicians including "approximately 30,000 additional reports as well as a number of special reports of both controlled and uncontrolled clinical experience" received by the firm since December, 1928, and photostat copies of forty-one letters from "leading authorities in the United States giving expression to the fact that they find Pyridium useful in their particular fields." The firm offered to tabulate the reports referred to but the Council considered the submitting of such a tabulation unnecessary, since they no doubt provide a type of evidence which has been abundantly supplied in connection with almost every sort of drug and has not been a dependable guide to wise and fair action on the part of the Council. As for the forty-one letters, they are, properly, brief statements of opinion in reply to an inquiry from the firm. All except two are favorable to Pyridium. These letters were not intended to supply evidence in the sense of detailed observation.

The firm, in addition, presented (*b*) new evidence in the form of published reports. The Council's referee analyzed these, as indicated in the second section of the addenda to this statement.

In its brief the firm pointed out technical faults and omissions of procedure in some of the laboratory investigations which had been cited in the former report as affording evidence unfavorable to Pyridium. The Council's referee was aware of these deficiencies when he reviewed the papers in question. It is correct, as pointed out by the firm, that the single 0.4 Gm. dose administered by Davis and Sharpe[6] is less than the repeated 0.6 Gm. dose recommended by the firm. In the opinion of the Council's referee, however, the experimental evidence presented justified the conclusions drawn from the work.

The firm presented a program of further research on Pyridium, prefacing it with the statement: "From our previous correspondence with the Council, we recognized the need for additional research on Pyridium." The program of research outlined by the firm appeared to the Council's referee to be comprehensive and admirable. The referee had no other suggestion to offer on this program. It is obvious that the results of the investigations will be awaited with interest and may afford a basis for renewed consideration of the drug. The present report of the Council is, of course, made without prejudice to future reconsideration of Pyridium.

6. Davis, Edwin, and Sharpe, J. C.: Urinary Antisepsis, J. A. M. A. **99**: 2097 (Dec. 17) 1932. (See also addendum 35.)

The firm requested the reacceptance of Pyridium, expressing the hope that "the Council will find sufficient basis for formulating conditions upon which to grant a continuance of the acceptance of Pyridium." After careful consideration of the material submitted by the firm, the Council concluded that, while Pyridium may have some value as an adjuvant in the treatment of genito-urinary infections, this is a very indefinite, indeterminable property of a substance recommended for its positive value as a urinary antiseptic.

The Council decided that there does not appear to be sufficient basis for the formulation of conditions on which to grant a reacceptance of Pyridium and voted to reaffirm its previous decision to omit Pyridium from New and Nonofficial Remidies and authorize publication of the foregoing statement of its consideration.

ADDENDA

I. Annotated List of Published Articles and Other Reports Consulted in 1932

An annotated list of the papers and reports studied by the present referee (except where otherwise noted) is as follows:

1. Ostromislensky, I.: Scientific Basis of Chemotherapy, 1926. Book. Bacteriologic and clinical data; unconvincing.

2. Belfield, W. T., and Rolnick, H. C.: Observations on the Physiology and Therapy of the Seminal Duct, J. A. M. A. **99**: 2104 (Dec. 17) 1927. Ingested and injected Pyridium excreted in seminal ducts. Spermatozoa stained. No therapeutic use of Pyridium reported here.

3. Hirschfelder, A. D., and Decherd, G. M.: Inhibiting Effects of Liquids upon Action of Antiseptics, Proc. Soc. Exper. Biol. & Med. **28**: 824-826, 1931. Bacteriostatic tests with B. coli and Staphylococcus aureus exposed for three hours to Pyridium in water solution and in solution with lipoids. Lipoids reduced the effect. Pyridium less bacteriostatic than acriflavine and mercuric chloride.

4. Pugh, W. S.: Infections of the Urinary Tract: The Use of Urinary Antiseptics. A. The Pyelonephritides, M. J. & Rec. **127**: 414-416 (April 18) 1928. Twenty cases reported in a summary table. Pyridium regarded as "helpful in cases without anatomical defect."

5. Meyers, J. L.: The Elimination of Dyes by the Uterine Mucosa, J. Lab. & Clin. Med. **14**: 936-939, 1928. Intravenously injected Pyridium stained the uterine mucosa of dogs. No data on concentration of dye in the mucosa. No clinical tests.

6. Wolhaupt, A. L.: Oral Therapy in the Treatment of Gonorrhea and Other Urinary Infections, M. J. & Rec. **128**: 272-273 (Sept. 19) 1928. Reports "personal experience with Pyridium as an adjuvant to local treatment." A preliminary report without much evidence presented, concluding that Pyridium is a promising therapeutic agent.

7. Bernhardt, E.: Neuere Farbstoff-behandlung (mit Pyridium) bei Ulcus molle und Gonorrhoe, Dermat. Ztschr. **58**: 397-402. Report on about twenty-one cases cured by Pyridium. Regards Pyridium as "unentbehrlich." Acute gonorrhea cured in fourteen days by oral administration. Observations seem to have been carefully made. Many details not presented. Not convincing, but of some value in favor of the drug.

8. Pugh, W. S.: Infections of the Urinary Tract: Prostatic Lesions, M. J. & Rec. **129**: 155-157 (Feb. 6) 1929. Oral administration of Pyridium plus massage "greatly reduces" the period of treatment of prostatitis. Good results claimed in acute posterior urethritis of gonococcal origin, in salpingitis and in vulvovaginitis of children. No data given.

9. Stern, R.: Klinische Erfahrungen mit Pyridium, einem neuen Harnantisepticum, Klin. Wchnschr. **8**: 1358-1359 (July 16) 1929. Report of three or four cases.

10. Stickl, O.: Ztschr. f. Desinfekt. u. Gesundhtsw. **21**: 33-37 (Feb.) 1929. Test tube bactericidal and bacteriostatic tests of solutions of Pyridium in salt solution and bouillon. Action decreased by presence of bouillon. In salt solution 1: 1,000 Pyridium killed Staphylococcus aureus "at once." Bacteriostatic action in dilution of 1: 10,000 at least. Much less effect on B. typhosus and B. pyocyaneus (1: 1,000 did not kill). Bacteriostatic action slight. Even less effect on B. anthracis. Bouillon reduced action as compared with salt. "Activity of Pyridium considerably less than that of a 1: 1,000 solution of corrosive mercuric chloride."

11. Thomas, B. A., and Wang, I. K.: Studies on the Comparative Clinical Values of So-Called Urinary Antiseptics, J. Urol. **22**: 22-41, 1929. Pyridium in solution in water was bacteriostatic for Staphylococcus aureus 1: 32,000 and for B. coli 1: 500; bactericidal for Staphylococcus aureus 1: 10,000 and for B. coli 1: 100. In solution in urine it was bacteriostatic for Staphylococcus aureus 1: 1,000 and for B. coli 1: 400; it was bactericidal for Staphylococcus aureus 1: 300 and for B. coli 1: 50. Sixty samples of urine containing the excreted dye after oral administration were studied. Six samples had some bacteriostatic action against Staphylococcus aureus and none for B. coli. None of the samples were bactericidal against either of these two organisms.

12. Walther, H. W. E.: Clinical Application of Urinary Antisepsis, South. M. J. **23**: 161-166 (Feb.) 1929. Tabulated report of fifty cases selected from a series of 200 cases of various sorts of urinary tract infection. Very favorable to Pyridium.

13. Bauereisen, A.: Zur Behandlung der Cystopyelitis mit Pyridium, Zentralbl. f. Gynäk. **54**: 2526-2530 (Oct. 4) 1930. Shows that 1: 1,000 solution of Pyridium in water killed B. coli in thirty minutes, and 1: 10,000 killed in twenty-four hours. Urine containing

excreted Pyridium was not bactericidal and only slightly bacteriostatic for B. coli. Argument presented for Pyridium "as an aid to the defenses of the body." Reports briefly result in about forty-two cases of cystonyelitis. Ranks Pyridium high as a urinary antiseptic. Very few data given.

14. Furniss, H. D.: Office Treatment of Urinary Tract in Women. Am. J. Surg. 5: 289-291 (Feb.) 1930. Pyridium thought to be effective in conjunction with other therapeutic measures.

15. Köster, O.: Bakteriologische und klinische Versuche mit Pyridium, München. med. Wchnschr. 77: 1013-1016 (June 13) 1930. States that a 1: 1,200 concentration of Pyridium can be reached in urine after ingestion of 0.6 Gm. daily. Maximum concentration reached on the second day. No killing of organisms in 300 minutes in a 1: 1,500 concentration of Pyridium excreted in urine, but some bacteriostatic action. Brief case reports on treatment of cystitis. Results favorable to Pyridium.

16. Mercier, O.: Le traitment des infection urinaires par les sels de pyridine, L' Union méd. du Canada 59: 739-742, 1930. Pyridium not referred to by name, but was evidently the substance used. The firm directed the referee's attention to this paper. Results of trials over a period of three years in 187 cases reported with very brief comments. No cure in any of 22 cases of acute gonorrhea and 26 cases of chronic gonorrhea. Complete cure of 38 per cent of 29 cases of cystitis. Cures of acute pyelitis in seven to nine days. "Brilliant results" when infection was due to Staphylococcus aureus. Chronic pyelitis cured in eighteen to eighty-six days. Considerable improvement in other cases. Failures in some. Pyridium an absolute failure in treatment of gonorrhea, but possibly beneficial in treatment of cystitis and pyelitis.

17. Neuberger, J.: Pyridium, ein neues Harndesinfiziens, München. med. Wchnschr. 77: 1016-1017, 1930. Brief comments on good results in treatment of cystitis and pyelitis.

18. Orlowski: Pyridium bei Störungen im Urogenitaltraktus, Ztschr. f. Urol. 24: 838-842, 1930. Brief reports on about forty-five cases of prostatitis, cystitis, mostly chronic and refractory to other treatment. "Miraculous results" in a number of cases. Pyridium a useful sedative. A man who could not drink beer at night without wetting the bed was cured of this notational enuresis by taking Pyridium and securing diuresis before he went to sleep! Good results claimed in treatment of gonorrhea. Says that Pyridium refutes Neisser's aphorism that "every case of gonorrhea gets well—except the first." There is a note by the editor (Dr. Casper) at the end of this paper, placed there with the consent of Orlowski, stating that Pyridium was no better than other urinary antiseptics.

19. Ravich, A., and Blaustein, L.: Study of 100 Suprapubic Prostatectomies, Long Island M. J. 24: 425-429 (Aug.) 1930. Pyridium used as part of preoperative preparation. Good results claimed, but there was no way of judging the effect of Pyridium among many other unknown factors.

20. Wolbarst, A. L.: The Study of a New Antiseptic in Urinary Infections, Internat. J. Med. & Surg. 43: 499-502, 1930. Favorable to Pyridium, but no new evidence presented. Reference to good results in use of Pyridium as an "adjuvant" to other methods.

21. Wolbarst, A. L.: Gonococcal Infection in the Male, 1930. Book. Pyridium decidedly effective as an adjuvant to local treatment of gonorrhea and "decidedly effective" as an "adjuvant to instrumental measures in pyelitis and other urinary tract infections of Staphylococcus and B. coli origin." Largely a quotation from Dr. Wolbarst's previous paper.

22. Weil, H.: Ueber die Anwendung des Pyridiums bei Gonorrhoe, Therap. d. Gegenw. 72: 455-459 (Oct.) 1930. Short reports on about 115 cases of gonorrhea, both acute and with complications. Pyridium an absolute failure here. No favorable results in treatment of B. coli cystitis with Pyridium. It presents strong evidence against Pyridium.

23. David, C.: Trois nouveaux antiseptiques urinaires, Hôpital 10: 282-284 (April, B). Pyridium cannot be used to replace local treatment. Mucosa of uterine cervix tinged yellow after oral ingestion of Pyridium. Not favorable to Pyridium.

24. Deakin, R. J.: The Efficacy of Pyridium in Gonococcal Urethritis, Missouri State M. A. 28: 123-125 (March) 1931. Average duration of treatment: 6 cases, local treatment alone, 109 days; 17 cases, local treatment plus Pyridium, 79 days. Selected cases. Conclusion reached that Pyridium aided treatment. At best this is favorable to Pyridium as an adjuvant.

25. Goerner, A., and Haley, F. L.: A Study of the Antibacterial Properties of Pyridium, Urinary Antiseptic, J. Lab. & Clin. Med. 16: 957-966 (July) 1931. Bactericidal and bacteriostatic tests of solutions of Pyridium in broth and urine. "Average bactericidal power" 1: 5,000, and "average bacteriostatic power" 1: 8,000. Bactericidal values below those obtained by expert. Inaccurate time of contact of Pyridium and bacteria accounts for this. This paper submitted by firm in typewritten form in 1931. Review shows that it is not strong laboratory evidence in favor of Pyridium and does not give any clinical information.

26. van den Bergh, A. A. H., and Revers, F. E.: Sulfhämoglobinämie nach Gebrauch von Pyridium, Deutsche. med. Wchnschr. 57: 706-708. Sulfhemoglobin formed when patients take Pyridium and magnesium sulphate at the same time. No clinical data given but reference made to studies by Revers and statement made that Pyridium is very useful for treatment of cystitis, pyelitis and prostatitis.

27. Mason, L. M.: Pyridium Therapy in Genito-Urinary Diseases, Virginia M. Monthly 58: 190-194 (June) 1931. Report on a two months clinical trial of Pyridium in treatment of prostatitis, pyelitis, pyelonephritis, gonorrhea and chancroids. Number of cases not recorded here. Brief abstracts of fourteen case records. Combinations of therapeutic measures used in nearly all. No clear evidence in favor of Pyridium, but author regards Pyridium as "decidedly effective as an adjuvant to instrumental measures in urinary infections."

28. Müller, F.: Erfahrung mit Pyridium bei septischer Erkrankungen, München. med. Wchnschr. 78: 233-235, 1931. Remarkably good results in treatment of peritonitis, appendicitis, perimetritis, pyosalpinx, postscarlatinal sepsis, puerperal infection with pelvic abscess, rheumatic fever (?). Single case of each reported. Surgery used in most of these cases, but not in all. The series is too small and uncontrolled to be worth much except as an indication of a possibility.

29. Schofield, F. S.: Typewritten reports, preliminary and supplementary, on "Clinical Observations on Pyridium," 1931. Work done at University of Pennsylvania Urological Department. Tests made at request of Merck & Co. As control, used previous study of 2,000 cases of gonorrhea treated at that clinic. Average duration of treatment by copaiba by mouth and irrigation with potassium permanganate was thirteen weeks. These reports show twenty cases of gonorrhea greatly improved in from four to six weeks and eleven other cases of various urinary tract infections improved by Pyridium. Dr. Schofield does not state his opinion and does not seem to have published these very good results. This paper published later.

30. Tatum, W. B.: Typewritten report sent in by the firm: "A Report of the Value of Pyridium in Forty-Eight Cases of Urinary Infection," 1931. Work done at the instigation of Merck & Co. "Varying good results" in many types of urinary tract infections. Elaborately documented. Long case report. Author concludes that "Pyridium has greatly benefited all cases treated and it has a definite place in urologic therapy as an antiseptic." This report is very difficult to summarize. It made a favorable impression.

31. Rosenthal, B.: Typewritten report submitted by the firm: "Dye Therapy in Chronic Prostatitis," 1931. Work done at the Gouverneur Hospital, New York. Combined Pyridium with other therapeutic measures in treatment of prostatitis and urethritis. Good results obtained. Abstracts of six case histories. Data scanty. Published Am. J. Clin. Path. 2, September, 1932.

32. Haley, F. L., and Goerner, A.: Typewritten report dated Nov. 25, 1930, submitted by the firm in 1931. Careful study of rate and amounts of excretion of Pyridium after oral administration. Possibility shown that excreted Pyridium differed from the Pyridium taken by mouth. Experiments showed that urines containing excreted Pyridium was bactericidal and bacteriostatic for B. coli and Staphylococcus aureus by prolonged contact of twenty-four hours or more. Inconclusive data on stimulation of wound healing by pyridium. These data impressed the referee favorably and still seem to have value in indicating that prolonged contact of bacteria with urine containing excreted Pyridium may kill or hinder the organisms. No reference to publication of this paper has been found.

33. Riahoff, P. J.: A Study of Pyridium as a Urinary Antiseptic, with Special Reference to Its Elimination by the Kidneys, J. Urol. 27: 329-342 (March) 1932. Report of careful work done under direction of Dr. Thomas and Dr. Kolmer at Pennsylvania. Pyridium had some bactericidal and bacteriostatic action against Staphylococcus aureus and B. coli in water and urine. But Pyridium excreted in the urine had no bactericidal or bacteriostatic effects on B. coli or Staphylococcus aureus. Strong acceptable evidence against Pyridium.

34. Gillespie, J. B.: Experiments on the Anti-bacterial Properties of Pyridium and Serenium, Proc. Staff Meet., Mayo Clin. 7: 372-373 (June 22) 1932. No bactericidal action on B. coli or Staphylococcus aureus by urine containing excreted Pyridium in concentrations of 1: 1,600 and 1: 8,000. No bacteriostatic action on B. coli and only slight on Staphylococcus aureus. Details of the bacteriologic methods used are not given. Presumably the bacteriologic work was satisfactory. This evidence is definitely against Pyridium.

35. Davis, Edwin, and Sharpe, J. C.: Urinary Antisepsis: A Comparison of Methenamine, Cystogen, Pyridium and Acriflavine as to Clinical Efficiency, J. A. M. A. 99: 2097 (Dec. 17) 1932. Pyridium given by mouth in 0.4 Gm. doses did not cause the secretion of any antiseptic in urine. B. coli grew luxuriantly in urine containing excreted Pyridium. Occasionally such urine decreased the growth of staphylococci but usually did not. The authors conclude that "Pyridium has practically no effect other than to color the urine." No clinical case reports in this paper.

II. Annotated List of Published Articles and Other Reports Consulted in 1933 After the Reply of Merck & Co. to the Report of the Council's Consideration of Pyridium

36. Schofield, F. S.: Specific Urethritis Treated with an Azo Dye, Pennsylvania M. J. 36: 15 (Oct.) 1932. This is the publication of the typewritten report reviewed in reference 29. The majority of cases of gonorrhea reported here were complicated. The value of Pyridium therapy was judged by "the time interval needed before the patient reached a quiescent stage in which it was deemed advisable to indicate prostatic massage or to search for other foci of infection." This averaged 24.9 days in a group of twenty patients. The referee is not convinced that the improvement noted was attributable to Pyridium. The cessation of injections, massage or the omission of urethral irrigations in acute gonorrhea established when a drug is given by mouth may be as helpful as the administration of the drug. Dr. Schofield does not report cures attributable to Pyridium, but improvement. At best, the drug appears from this to be a beneficial adjuvant.

37. Courtiss, M.: Antiseptics—Pyridium in Kidney and Bladder Infections in Pregnancy, typewritten copy of a report from the Massachusetts Memorial Hospital in June, 1932. Considerable amount of clinical material relating to 137 cases of pyelitis and cystitis. Eighty per cent of patients cured; 94 per cent relieved. Infection recurred in some cases. Lacks observations on untreated cases and lacks consideration of the expected postpartum improvement of infections occurring during pregnancy. Referee not convinced that Pyridium cured 80 per cent of these patients.

38. Goerner, A., and Haley, F. L.: The Penetration of Pyridium into the Tissues of the Genito-Urinary Tract, report from the Long Island College Hospital, Sept. 21, 1932. Results showed penetration of the dye into the tissues. No proof that the amount and character of the compound in the tissues has antiseptic and therapeutic effects. Penetration has been previously considered by the Council, as stated in this abstract.

39. Marion, D., and Magnan, L. A.: Union méd. du Canada 61: 1061 (Sept.) 1932. Typewritten translation supplied by the firm. Record of results in "The Use of Pyridium in Obstetrics and Gynecology." Cases of gonorrhea, pyelitis, cystitis, cervicitis and salpingo-ovaritis. "Preliminary work" indicating possible value of Pyridium. Referee not convinced by the evidence.

40. Brown, T. K.: Bacteriological Study of Urinary Infection in Pregnancy and Puerperium, with Special Reference to the Use of Pyridium, from the Department of Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, 1932. Pyridium found to have some value in combating infections of the kidney due to staphylococci. Pyridium so ineffective in cases of pyelitis and cystitis due to colon bacilli that methenamine was prescribed as a routine along with Pyridium in mixed colon bacillus and staphylococcic infections. Symptomatic improvement with Pyridium therapy in colon bacillus infections, but the "offending organism" persisted.

AZOPHENE (MALLOPHENE) NOT ACCEPTABLE FOR N. N. R.

In April, 1932, Azophene (formerly called Mallophene) was presented by the Mallinckrodt Chemical Works, St. Louis, for consideration of the Council as beta-phenyl-azo-alpha-alpha-diamino-pyridine hydrochloride. It was proposed for use topically and orally as a genito-urinary antiseptic. Examination by the A. M. A. Chemical Laboratory had shown it to be identical with Pyridium (Collins, G. W.: *J. Am. Pharm. A.* 20:445, 1931). Since Pyridium already stood accepted, the Council considered accepting Azophene but postponed action until further investigation and disposition of questions which had arisen concerning the former.

Subsequently the Council, as a result of extended investigation, declared Pyridium unacceptable for continued inclusion in New and Nonofficial Remedies because the claims advanced for it as a local, general, or urinary antiseptic are unwarranted (See report on Pyridium). In accordance with its original policy of considering Azophene and Pyridium as identical, and since, to the Council's knowledge, there exist no reports indicating that the former is superior in any way to the latter, the Council declared Azophene unacceptable for New and Nonofficial Remedies because claims for its usefulness as a local, general or urinary antiseptic are unwarranted.

Committee on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COMMITTEE ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOLLOWING ANY NECESSARY CORRECTIONS OF THE LABELS AND ADVERTISING TO CONFORM TO THE RULES AND REGULATIONS. THESE PRODUCTS ARE APPROVED FOR ADVERTISING IN THE PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION, AND FOR GENERAL PROMULGATION TO THE PUBLIC. THEY WILL BE INCLUDED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED BY THE AMERICAN MEDICAL ASSOCIATION.

RAYMOND HERTWIG, Secretary.

TIDAL WAVE CORN MEAL

Manufacturer.—Texas Star Flour Mills, Galveston, Texas.

Description.—Finely granular white corn meal practically free from corn germ and bran.

Manufacture.—The manufacture is essentially the same as that given for Ambrosia Cream Corn Meal (THE JOURNAL, Oct. 28, 1933, p. 1393) with the exception that all the corn grits stock is reduced and blended together to make the final meal.

Analysis (submitted by manufacturer).—

	per cent
Moisture	13.0–14.5
Ash	0.9– 1.0
Fat (ether extraction method)	2.5– 3.2
Protein (N × 6.25)	7.9– 8.4
Crude fiber	1.8– 3.0
Carbohydrates other than crude fiber (by difference)	73.9–69.9

Calories.—3.5 per gram; 99 per ounce.

IRRADIATED VITAMIN D PASTEURIZED MILK

Distributor.—Kennedy-Mansfield Dairy Company, Madison, Wis. (subsidiary of The Borden Company, New York).

Description.—Bottled pasteurized vitamin D milk irradiated by Steenbock process (patent No. 1,680,818).

Preparation.—Milk is irradiated by a "CP Carbon Arc Lamp Milk Irradiator" equipped with recording meters for measuring lamp energy input, output of milk pump, and ultraviolet ray emanations of the arc lamps, which provide complete charts of operation for inspection by plant and health officials. The irradiated milk is pasteurized by standard procedure (holding method, thirty minutes at 63 C.), immediately cooled, automatically bottled and capped.

Vitamins.—Clinical investigation shows this irradiated milk to be a reliable antirachitic agent protecting practically all infants excepting those prematurely born; contains 50 Steenbock vitamin D units per quart.

Claims of Distributor.—Irradiated antirachitic pasteurized milk having otherwise the natural flavor and food values of usual pasteurized milk. Complies with the requirements of the state of Wisconsin and the health department of the city of Madison. The method of irradiation and the equipment are under scientific control.

KRASDALE TOMATO JUICE

Distributor.—A. Krasne, New York.

Packer.—Edgar F. Hurff, Swedesboro, N. J.

Description.—Canned pasteurized tomato juice with added salt; retains in high degree the natural vitamin content; the same as the accepted Hurff Brand Tomato Juice (THE JOURNAL, March 18, 1933, p. 818).

VITAMIN D FORTIFIED PASTEURIZED MILK SCOTT-POWELL

Distributor.—Scott-Powell Dairies, Philadelphia.

Description.—Bottled pasteurized grade B milk fortified with vitamin D (vitamin D concentrate prepared from cod liver oil); contains 150 vitamin D Steenbock units per quart.

Preparation.—The milk complies with the requirements specified by the laws of the states of Pennsylvania and New Jersey and the cities of Philadelphia and Gloucester and other municipalities in which it is distributed.

See this section for Vitamin D Fortified Pasteurized Milk of W. J. Kennedy Dairy Company, Detroit, for description of fortification with vitamin D (THE JOURNAL, July 1, 1933, p. 34). The milk is pasteurized by the standard procedure of holding at 62 C. for not less than thirty minutes, is immediately cooled to 3 C., and automatically bottled.

Analysis (submitted by manufacturer).—

	per cent
Moisture	87.2
Total solids	12.8
Ash	0.7
Fat	3.9
Protein (N × 6.38)	3.5
Lactose (by difference)	4.7

Calories.—0.7 per gram; 20 per ounce.

Vitamins.—The vitamin D concentrate used in the preparation of this vitamin D milk and the fortified milk are regularly tested biologically. Clinical investigation shows this milk to be a reliable antirachitic agent.

Claims of Manufacturer.—A vitamin D fortified, antirachitic pasteurized milk having the natural flavor and food values of standard pasteurized milk.

(1) G. W. C. BRAND AMBER TABLE SYRUP
(2) IOWA MAID AMBER TABLE SYRUP
(3) MINNEOPA BRAND AMBER TABLE SYRUP
(4) VALLEY QUEEN BRAND AMBER TABLE SYRUP

(CORN SYRUPS FLAVORED WITH REFINERS SYRUP)

Distributors.—(1) Grocers' Wholesale Company, Des Moines, Iowa.

(2) Charles Hewitt & Sons Company, Des Moines, Iowa.

(3) Bismarck Grocery Company, Bismarck, N. D.

(4) Wilson Mercantile Company, Wausau and Rhinelander, Wis.

Packer.—Wheeler-Barnes Company, Minneapolis.

Description.—Table syrup; corn syrup base (85 per cent) with refiners syrup (15 per cent); the same as the accepted Golden Oak Brand Amber Syrup (THE JOURNAL, Dec. 3, 1932, p. 1948).

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SATURDAY, DECEMBER 30, 1933

THE RESPONSIBILITY OF THE PHYSICIAN IN THE PREVENTION, DIAGNOSIS AND TREATMENT OF CANCER

Cancer, it has been said, is an unsolvable problem; certainly for the problem of the cause of cancer not even an approximate solution is available. Indeed, the great central problem of life and cell growth has not yet been solved. Whether these problems are unsolvable, no one knows. The advance of biologic science is marked by efforts to explain the succession of phenomena that are laid bare as investigation proceeds rather than by the complete understanding of basic biologic problems in the final sense. In this gradual progress of science, results of great practical importance are achieved from time to time. The discovery of the tubercle bacillus did not solve the problem of tuberculosis, but it did show the right way for further study and for better control of the disease. How the bacillus produces disease and how the body reacts against the bacillus are still largely unsolved problems. The fact is that science provides no complete, no ultimate explanation of any disease; hence little wonder that the problem of cancer remains unsolved.

Notwithstanding the slowness of scientific progress, the knowledge of cancer is actually growing. The truth is that more advance has been made in detailed knowledge of cancer during the last two or three generations than in all previous time. The details of this new knowledge need not be reviewed item by item. The practical outcome is that, while any complete understanding of cancer has not been reached, the power of medicine to prevent, to diagnose and to treat cancer has been increased enormously. And the responsibilities of the physician with respect to cancer have increased likewise. On him rests primarily the duty to make sure that the individual patient receives the benefit of the knowledge and the measures that tend to prevent cancer. Briefly, prevention of cancer rests mainly on the avoidance and removal of "local irritation." Just how "local irritation" acts to cause cancer is not known, but there is no doubt that it may lead to cancer. Of the tissues liable to such irritations and chronic inflammations may be mentioned the uterine cervix with its lacerations and "chronic cervicitis," the skin and its moles and ulcers, the mouth, the tongue, the mucocutaneous junctions, the breast and the prostate with their chronic hyperplastic inflammations. Here is indeed a wide field for constant preventive efforts by the progressive, cancer-conscious physician.

Self evidently, on the physician rests also the main responsibility for the early diagnosis of cancer, on which in turn depends the outcome of its treatment. In connection with this matter, of such vital significance to the individual patient, the physician must consider thoroughly and conscientiously such questions as these: Has he formulated for himself a wise and practical plan for action in all cases in which the question of cancer may arise? Are his regular patients likely to report to him promptly the appearance of any suggestive symptom or sign? If not, why not? Is he fully prepared to take without delay the necessary steps, either by himself or through competent consultants, to secure the final diagnosis in a given case with a doubtful lesion? Does he realize fully that it may be a fatal error to tell a patient with a suggestive lump or lesion somewhere "to forget it and come back next month"? Are the services of a competent pathologist readily available and will adequate specimens for microscopic diagnosis reach the pathologist promptly and in the proper state of preservation? Are the special experts to whom he may refer cases for diagnosis and treatment fully equipped in all respects for prompt and efficient service? Does he accept in its full meaning the statement that the treatment of cancer, surgical as well as radiologic, should be entrusted only to those who have adequate skill and experience? These are questions that the physician must answer in a practical and trustworthy manner if he is to meet his responsibility with respect to cancer as now understood. Better control of cancer by prevention, early diagnosis and prompt treatment rests with the physician.

DINITROPHENOL AND ACCELERATED TISSUE METABOLISM

The discovery of a drug that gives promise of therapeutic usefulness is always an event of interest in medicine. Careful investigation and cautious clinical trial are indispensable before widespread application is undertaken. There have been few therapeutic innovations that have not sooner or later been found to present some limitations to their unqualified practical usefulness or even to involve unanticipated hazards to health. That is why it is extremely important to learn every ascertainable detail of the pharmacodynamic action of new products as early as possible. The problems of the range between useful and lethal doses, the causes of death, and possible antidotes must be considered with great care. This statement may be applied specifically

to 1-2-4 dinitrophenol, a substance demonstrated only a few months ago to produce fever in experimental animals.[1] The observation that this compound can increase the metabolic turnover at once suggested its resemblance to well known stimulants of oxidative metabolism, such as the hormones thyroxine and epinephrine.

The questions raised by the study of dinitrophenol, notably at the Stanford University School of Medicine in San Francisco, have already been considered to some extent in THE JOURNAL.[2] Investigation of its pharmacologic properties shows that it has the power to increase metabolism to high levels without causing important damage to vital organs and functions. Serious harm is apparently caused by the drug only in large doses, which produce too great metabolic stimulation with resulting fever. In low, or therapeutic, doses, the metabolism may be increased 50 per cent or more over considerable periods without unpleasant symptoms or toxicity. Such an action is useful in treating obesity, since the increased metabolism results in loss of weight, just as it does with thyroid medication. As a suitable regimen of dinitrophenol medication for adults there has been suggested, on the basis of the early clinical trials in the reduction of obesity, an initial daily dose of 100 mg. of the sodium salt orally, taken with meals, with an increase at weekly intervals until a dose is established that causes a loss of body weight of between two and three pounds weekly or too severe or unpleasant symptoms of warmth and sweating. Such a procedure has been reported to be free from demonstrable evidences of cumulative or toxic effects. Certain limitations, however, apply to a few susceptible persons.

More detailed information as to the precise function of dinitrophenol is now available.[3] All of the disturbances provoked by the administration of dinitrophenol are attributable to a single primary action, that of accelerating the rate of oxidative metabolism. The magnitude of this acceleration may approach values attained physiologically only under conditions of vigorous muscular exercise and far exceed those resulting from administration of the hormones normally concerned with the regulation of metabolism, thyroxine and epinephrine. Specifically, the increase in oxygen consumption may amount to more than ten times the resting rate. The studies at Stanford University show that the rise in body temperature that follows the increase in oxygen consumption is secondary to the acceleration in metabolism. During the action of the drug, pronounced decreases occur in liver and muscle glycogen, while blood sugar and lactates and muscle lactates tend to rise. The total carbohydrate disappearing, however, accounts for less than half of the oxygen consumption. The principal fuel of the accelerated metabolism must therefore be other than carbohydrate. As there seems to be no increase in urinary nitrogen output, one may assume that fat is lost from the body. Such observations fail to reveal any differences between the "excess" metabolism of dinitrophenol and that occurring normally. Danger arises when the waste heat cannot be effectively disposed of. Dinitrophenol is rapid in action compared to thyroxine; it apparently does not exhibit the complication of sympathetic stimulation so characteristic of epinephrine. With fatal doses of the new drug, a decrease in respiration and oxygen consumption occurs shortly before death. At this time lactates rise and the carbon dioxide combining power and the p_H of the blood fall, indicating the development of a premortal anoxemia and acidosis. However, with nonfatal doses, none of these phenomena appear. Suitable cautions have already been given in THE JOURNAL; they warrant repetition. The drug must be sufficiently pure; it has been stated that much of the material on the market is not sufficiently pure. Aside from the skin reactions, the chief danger from this drug is in the indiscriminate or careless overdosing that may result from its sale to the public. It has already been demonstrated that an overdose of sufficient size will cause a fatal pyrexia in man, just as it does in experimental animals. That an overdosage may be toxic does not constitute a sufficient reason for not using dinitrophenol any more than for any one of many potent drugs commonly employed by physicians, but it does indicate that the treatment must be directed by the physician. For maximal safety the initial dose of dinitrophenol should be small, and increasing doses may be employed only as the clinical response seems to warrant.

1. Cutting, W. C., and Tainter, M. L.: Actions of Dinitrophenol, Proc. Soc. Exper. Biol. & Med. **29**: 1268 (June) 1932.
2. Cutting, W. C.; Mehrtens, H. G., and Tainter, M. L.: Actions and Uses of Dinitrophenol, J. A. M. A. **101**: 193 (July 15) 1933. Tainter, M. L.; Stockton, A. B., and Cutting, W. C.: Use of Dinitrophenol in Obesity and Related Conditions, ibid. **101**: 1472 (Nov. 4) 1933. The Toxicity of Dinitrophenol, Current Comment, ibid. **101**: 1080 (Sept. 30) 1933.
3. Hall, V. E.; Field, J. 2d; Sahyun, M.; Cutting, W. C., and Tainter, M. L.: Carbohydrate Metabolism, Respiration and Circulation in Animals with Basal Metabolism Heightened by Dinitrophenol, Am. J. Physiol. **106**: 432 (Nov.) 1933.

"AVAILABLE" IRON IN THERAPY

The question of the type of compound to be preferred for use in therapy with iron has been the subject of debate for many, many years. Empirically, the inorganic salts of the element found widespread use long before the end of the last century. During that period, distinctions began to be made between so-called organic and inorganic combinations of iron. The term "masked iron" was sometimes given preference over the expression "organic iron." From the latter point of view the acetate and albuminate of iron, for example, were both classified with inorganic iron because they are capable of dissociation and the iron therein is precipitated by ammonium sulphide. Many sources of "food iron," that is, iron as it is present in common food materials such as the yolk of egg, appeared to belong to the category of "masked iron." At one period it was widely believed that "food iron" and related

compounds of the element possess a pronounced advantage from the point of view of readiness of absorption and assimilation. In the course of time, however, the pendulum swung away from this extreme view, leaving the conviction among most critical students of the subject that inorganic iron follows the same course as the food iron. At any rate, there was abundant experimental evidence that inorganic iron can function for the hematopoietic needs of the body.

The more recent investigations of the control of nutritional anemias produced in animals by the use of exclusive milk diets have given a new impetus to the critical consideration of iron therapy, particularly in hypochromic anemia. The contributory rôle of copper represents a new phase of the subject, though it does not fundamentally alter the place of iron. In the case of adults, at least, copper seems to be sufficiently ubiquitous, in the traces that may be requisite, to exclude it from serious consideration in the usual therapeutic routine. Of late, ferric ammonium citrate, used in large daily doses amounting usually to as much as from 4 to 8 Gm., has attained widespread vogue for reasons that are by no means obvious. Many of the formerly popular soluble iron salts seem to have become outmoded.

The availability of iron compounds to an anemic animal can be ascertained by a study of the rate of hemoglobin formation (in the presence of sufficient copper) or by the amount of iron stored in the liver. Recent tests of the former type have been made by Elvehjem, Hart and Sherman[1] at the University of Wisconsin. They show that the iron in a variety of soluble, readily dissociated salts is utilized with practically equivalent ease. This applies, for example, to ferric chloride, ferric pyrophosphate, ferric hypophosphite and ferric glutamate. Elvehjem, Hart and Sherman point out that this does not mean that all the available compounds are equally valuable. Other properties, such as taste and toxicity, are important factors. They have found that ferric pyrophosphate possesses many fine qualities. The iron in pyrophosphate not only is available but is held in such firm combination that it does not produce the astringent effects so characteristic of other iron salts. This salt, they add, may also be valuable in cases of anemia with achlorhydria, because it is soluble in neutral solutions and may be more readily assimilated in the absence of hydrochloric acid.

The Wisconsin biochemists have also made a real contribution to the comparative value of ordinary foods as sources of iron. This cannot be based on their total chemically assayed iron content. Each food contains a portion of iron that is readily utilized for hemoglobin formation and a portion that is unavailable and may consist mainly of hematin compounds. This may help to explain why certain iron salts appear to be superior to food iron in the treatment of responsive anemias. Elvehjem, Hart and Sherman have found that the available iron in foods can be estimated "with a fair degree of accuracy by relatively simple methods, such as Hill's dipyridyl procedure.[2] On this basis about one half of the total iron of such products as wheat, oats and yeast is "available" iron. The Wisconsin investigators have concluded that various forms of nonhematin iron, even insoluble salts, are much superior to hematin compounds (organic iron) as a source of iron for the body. Hematin compounds, they state, have no place in the group of therapeutic agents used for hypochromic anemias. Further research along these lines serves to dispel a considerable number of current prejudices, claims and misconceptions as well as to promote more rational practices in the domain of iron therapy.

1. Elvehjem, C. A.; Hart, E. B., and Sherman, W. C.: The Availability of Iron from Different Sources for Hemoglobin Formation, J. Biol. Chem. **103**: 61 (Nov.) 1933.

2. Hill, R.: Proc. Roy. Soc. London, Series B **107**: 205, 1930.

Current Comment

THE CLINICAL PATHOLOGIST AS A TEACHER

The evolution of the clinical laboratory in the modern hospital constitutes one of the remarkable advances of the present century. The hospital laboratory is often the axis about which the scientific work of the institution revolves. In his presidential address before the recent annual meeting of the American Society of Clinical Pathologists, Walter M. Simpson[1] directed particular attention to the rôle of the clinical pathologist as a teacher. On the clinical pathologist, he pointed out, devolves a large share of the responsibility for the correlation and dissemination of the scientific aspects of hospital medical practice. The teaching activities of the alert clinical pathologist may assume several forms. A cheerful willingness to give a correct interpretation to laboratory results in the light of clinical observations constitutes one of the most fruitful forms of medical teaching, particularly as related to the welfare of the patient. The hospital staff conference and the clinicopathologic conference provide perhaps the best opportunities for the pathologist to contribute a large share to postgraduate medical education. The well directed clinicopathologic conference makes available the university idea of postgraduate medical education in every hospital that has a capable clinical pathologist. It is Simpson's belief that the clinical pathologist who does not fulfil this duty is missing his greatest opportunity to gain the respect and confidence of his medical brothers. Such conferences are capable of providing constant stimuli to the scientific activities of the hospital. Intelligent correlation and interpretation of the information gained by postmortem examinations will quite naturally create interest in morbid anatomy. The clinician is thus provided with a real incentive to obtain permission for postmortem examinations on his patients.

1. Simpson, W. M.: The Clinical Pathologist as Consultant and Teacher, Am. J. Clin. Path. **3**: 327 (Sept.) 1933.

The successful conduct of clinicopathologic conferences requires consummate tact. If the emphasis is placed too heavily on postmortem pathology at the expense of practical clinical aspects, the interest of the average practitioner will not be aroused. Attendance at the clinicopathologic conference should be optional and induced only by the excellence of the program. Such conferences should be held often enough to sustain interest. The weekly or biweekly clinicopathologic conference, lasting for an hour or an hour and a half, but not longer, will accomplish this end. The logical place for the conference is at the hospital. The time for the conference should be chosen with a view to inconveniencing the smallest number of persons. The programs should be arranged so that a wide variety of subjects may be discussed at each conference, in order that physicians in special fields may be induced to attend the conferences regularly. Recurring discussion of commonly encountered diseases is of much greater importance than emphasis on the presentation of rare and unusual ones. The clinical pathologist is the natural and logical director of such conferences. While it is generally admitted that the pathologist is usually "the court of last appeal," the shrewd and tactful pathologist will rarely exercise this prerogative. To give instruction to the informed physician is a different matter from teaching the uninformed layman or medical student. The exercise of restraint will often accomplish much more than a practice of forcing his opinions and decisions on his fellow practitioners.

FEDERAL MEDICAL RELIEF AND EMPLOYEES' COMPENSATION

In these trying times, actions ensue so rapidly in Washington that it is increasingly difficult for a medical journal, published weekly, to keep its readers abreast of the last minute advice regarding their relationship to government activities. Last week THE JOURNAL published an extended statement concerning 4,000,000 workers involved in the Civil Works Administration. It pointed out that apparently these 4,000,000 workers had been placed under the coverage of the Federal Employees' Compensation Act and that therefore they would be entitled to medical care in government hospitals and from government physicians for every injury and occupational disease sustained in the performance of duty. Now comes a revision of the original rules and regulations with a statement that it is retroactive to November 16. Apparently, employees of the Civil Works Administration may have the right to choose their own physicians under such circumstances. The new regulation states specifically that the benefits provided are not intended to be payable as compensation under the United States Employees' Compensation Act. A protest by the Indiana State Medical Association directly to the President of the United States and to the United States Employees' Compensation Commission, accompanied by a similar protest by the director of the Unemployment Relief Commission of that state, brought a reply indicating that all reputable physicians willing to give treatment at reasonable charges may be used for the care of employees of the Civil Works Administration. Moreover, the director of relief was authorized to notify local administrators at once that they are authorized to advise the local medical profession accordingly and to make arrangements to permit reputable private physicians to participate in rendering this service in places in which government medical officers and hospitals are not available and reasonably accessible. As long as the latter rule is in effect it will operate as a bar to the free choice of physicians by injured employees in such places as can make available government service. In the meantime, the American Medical Association has called the situation to the attention of the Federal Civil Works Administrator, urging him to abolish the limitations described and to amend the regulation so as to permit employees to select their own physicians either from all doctors of medicine licensed to practice or else from lists of physicians approved by the United States Employees' Compensation Commission.

Association News

THE CLEVELAND SESSION

Authorization of a Symposium on Amebic Dysentery in the Scientific Exhibit

The Committee on Scientific Exhibit of the Board of Trustees has authorized a symposium on amebic dysentery in the Scientific Exhibit at the Cleveland Session, June 11-15, 1934. The sections of the Scientific Assembly taking part are the Section on Practice of Medicine, the Section on Gastro-Enterology and Proctology, the Section on Pathology and Physiology, the Section on Pharmacology and Therapeutics, and the Section on Preventive and Industrial Medicine and Public Health. The symposium will consist of a group of exhibits dealing with the diagnosis, treatment and prevention of amebic dysentery. Application blanks for space may be obtained from the Director, Scientific Exhibit, American Medical Association, 535 North Dearborn Street, Chicago.

MEDICAL BROADCAST FOR THE WEEK

Talks over Network of the National Broadcasting Company

The American Medical Association broadcasts each Monday afternoon from 4:45 to 5 o'clock, Eastern standard time (3:45, central standard time). There will be no talk on Monday, January 1. The next talk over the National Broadcasting Company network will be on January 8.

Radio Talks from Station WBBM

The American Medical Association broadcasts on Tuesday and Thursday mornings from 8:55 to 9 o'clock, central standard time, over Station WBBM (770 kilocycles, or 389.4 meters).

The subjects for the week are as follows:

January 2. Pasteurized Milk.
January 4. Health Resolutions.

There is also a fifteen minute talk sponsored by the Association on Saturday morning from 9:45 to 10 o'clock over Station WBBM.

The subject for the week is as follows:

January 6. Fermentation and Disease.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION, PUBLIC HEALTH, ETC.)

ARKANSAS

Society News.—Among others, Dr. Earle H. Hunt, Clarksville, spoke before the Ninth Councilor District Medical Society in Harrison, December 5, on "Vomiting in Pregnancy."——Dr. Benjamin H. Hawkins, Mena, among others, addressed the Sixth Councilor District Medical Society in DeQueen, November 28, on "Lethargic Encephalitis."

Antimalaria Campaign Started.—With the appointment of Dr. William B. Grayson, Little Rock, state health officer, as state director of malaria control work, November 29, the statewide campaign in Arkansas was inaugurated. Work was begun at several places, December 4. The state has been divided into five districts. Salaries and wages will be paid by the Civil Works Administration, while expenses for materials and supplies will be borne by the U. S. Public Health Service.

CALIFORNIA

Lectures on the Heart.—The Los Angeles County Heart Association conducted a series of lectures on heart disease in Los Angeles, December 7-8, the first three sessions of which were joint meetings with the Los Angeles County Medical Association. Dr. Frank R. Nurum, Santa Barbara, was the guest speaker, on "The Use of Tissue Extracts in Angina Pectoris and Spastic Arterial Disease." Local physicians participating in the program were Drs. Edward Richmond Ware, R. Manning Clarke, Phillip E. Rothman, Henry H. Lissner, Donald J. Frick, Burrell O. Raulston, John C. Ruddock, Howard F. West, Robert W. Langley, William H. Leake and Arthur Stanley Granger.

CONNECTICUT

Beaumont Exhibit.—A collection of all the editions of the work of Dr. William Beaumont on the physiology of digestion, and other documents and memorabilia having to do with his life are on display at Yale University School of Medicine, in recognition of the centenary of the publication of "Experiments and Observations on the Gastric Juice." Included in this collection are two copies of the first edition, published by Allen in Plattsburgh, 1833, one of them in the original cover; a copy of the first edition published in Boston, 1834; a first edition of Combe's reprint, Edinburgh, 1838; a copy of the second edition, published by Goodrich in Burlington, 1847; a first edition of the German translation, Leipzig, 1834, and two copies of the first edition of the facsimile, reprinted in Boston, 1929, on the occasion of the thirteenth International Physiological Congress. There are photostatic copies of Beaumont's license to practice medicine, granted in June, 1812, by the Third Medical Society of the State of Vermont; Beaumont's commission as surgeon of the U. S. Army, signed by President John Quincy Adams in 1828, and an early comment of Beaumont on the case of Alexis St. Martin, on whom his experiments with gastric juice were performed, published in the *Philadelphia Medical Journal* in 1826. The original letter sent by Beaumont in 1834 to Hezekiah Howe, New Haven book dealer, is in the collection. In this letter he says:

> Will you please to let me know what number of copies of my "Experiments and Observations, etc." you may have remaining on hand unsold, soon as convenient? I shall probably have occasion to recall all surplus books from the Eastward to supply the Western market, my depot there having become nearly exhausted and the demand for them continuing.

The exhibit includes a letter from Benjamin Silliman, professor of chemistry at Yale, to Beaumont in 1823, which gives directions for sending a specimen of gastric juice to Prof. Jacob Berzelius in Sweden. There is also a volume of Proceedings of the Connecticut Medical Society in which reference is made to the election of Dr. Beaumont as an honorary member in 1833 and an account is given of his appearance before the society to demonstrate his patient in 1834.

FLORIDA

County Society Organizes Credit Bureau.—Members of the Orange County Medical Society recently organized the Orange County Credit and Collection Bureau in Orlando. A state charter has been granted and the incorporators are Drs. Calvin D. Christ, chairman; Horace A. Day, vice chairman; John R. Chappell, secretary; John S. McEwan, Lawrence C. Ingram, Meredith Mallory and Samuel A. Shoemaker. Credit rating of prospective patients will be made available to members of the society, and the bureau will serve as a clearing house for the physicians' accounts.

ILLINOIS

Society News.—Dr. Ernest Sachs, St. Louis, spoke before the St. Clair County Medical Society in Belleville, December 6, on "Diagnosis and Treatment of Brain and Spinal Cord Injuries."——Dr. Joseph L. Miller, Chicago, was among the speakers at the meeting of the Tri-County Medical Society (Henry, Knox and Warren), November 16; his subject was treatment of migraine.

Reserve Officers' Reception.—The Cook County chapter of the Reserve Officers Association of the United States will give a reception in honor of Major General and Mrs. Preston Brown at the Army and Navy Club, January 6. All reserve officers, whether members of the association or not, are cordially invited and asked to bring, as their guests, ladies and also prospective members of the officers' reserve corps. Further particulars may be obtained from Col. Gilbert Fitz-Patrick, 185 North Wabash Avenue, Chicago, or from the headquarters of the association, 53 West Jackson Boulevard.

State Advisory Board in Public Health.—At the first meeting of the state board of public health advisers, December 4, called by the state health commissioner, three committees were appointed to work out details and recommend practicable programs for dealing with heart disease, amebic dysentery and trachoma. It was recommended at this meeting that the state department of health discontinue its treatment of patients with trachoma and restrict its activities in this connection to education in preventive practice. The promotion of prophylaxis against diphtheria and typhoid and the early adoption of a vigorous state-wide program for the control of heart disease were urged.

Chicago

Dr. Doan to Lecture on Leukopenias.—Dr. Charles A. Doan, professor and head of the department of medical and surgical research, Ohio State University School of Medicine, will present an address before the Chicago Medical Society, January 10, on "Leukopenias from the Standpoint of the General Practitioner." January 14, the society will hold a memorial meeting in honor of its founder, Dr. Nathan S. Davis. The speaker will be Dr. James B. Herrick.

Course in Ophthalmology.—Beginning January 1, a course on ophthalmology will be carried on in the hospitals of Chicago for interns and residents in this specialty, it has been announced. Two hundred hours of instruction will be given by fifty-three instructors from the universities and hospitals in the city, the lectures to be divided evenly between the fundamental and the clinical branches. Practically all the lectures will be delivered at the Illinois Eye and Ear Infirmary.

Society News.—Speakers before a joint meeting of the Chicago Roentgen Society and Chicago Orthopedic Club, December 14, included Drs. Julius Brams on "Congenital Absence of the Femur" and Charles N. Pease, "Injuries to the Intervertebral Disk and Vertebra Following Lumbar Puncture."——Among other speakers, Dr. Joseph Greengard spoke on "Comparative Tuberculin Tests in Children" before the Chicago Tuberculosis Society, December 14.——Dr. John Philip Sandblom, Orebro, Sweden, among others, spoke at a meeting of the Chicago Society of Internal Medicine, December 18, on "Physiology of the Human Gallbladder Studied in Connection with Blood Transfusion and After Stomach Operations."——Speakers before the Chicago Gynecological Society, December 15, were Drs. George T. Palmer, Springfield, on "Tuberculosis in Its Relation to Pregnancy," and Irving F. Stein, "Oxygen Pneumoperitoneum in the Diagnosis and Treatment of Tuberculous Salpingitis."

INDIANA

Society Anniversary.—The eighteenth annual meeting of the Indiana Society for Mental Hygiene, December 4, was an observance of the twenty-fifth anniversary of the mental hygiene movement. Among the topics discussed were "The Mental Hygienist's Attitude Toward Birth Control," "Conservation and Prevention," "Mental Hygiene and Education" and "Mental Hygiene and Crime." Speakers included Drs. Charles P. Emerson, Indianapolis; S. Spafford Ackerly, Louisville; Louis A. Lurie, Cincinnati, and Olga Hoffman, Madison.

KENTUCKY

Lectures for Practitioners.—The Franklin County Medical Society was host for a course of lectures conducted under the auspices of the Kentucky State Medical Association at Frankfort, November 23. Drs. Emmet F. Horine and Owsley Grant, both of Louisville, spoke on heart disease and prostatic and kidney diseases, respectively. The lectures were illustrated with motion pictures and slides and each was followed by discussion. A similar course was held in Williamstown for Grant County physicians in October by Drs. Virgil E. Simpson and Frank P. Strickler, Louisville. Discussions were presented on disease of the thyroid and of the gallbladder.

Society News.—A symposium on the thyroid gland was presented before the Jefferson County Medical Society, Louisville, October 2, by Drs. Adolph O. Pfingst, R. Alexander Bate and William O. Johnson. At a combined meeting with the Louisville District Dental Society, October 16, speakers were Dr. John Stites, on "Dental Infections as Related to the Field of Medicine" and Orville B. Coomer, D.D.S., "The Growing Interdependence of Medical and Dental Practice."——Dr. William R. Davidson, Evansville, Ind., among others, addressed the semiannual meeting of the Southwestern Kentucky Medical Association at Marion, October 24, on "The Infected Hand."

MARYLAND

Society News.—Dr. Simon Flexner, New York, addressed the annual meeting of the Baltimore City Medical Society, December 1, on "Poliomyelitis and Other Virus Infections of the Central Nervous System."——At a meeting of the Allegany-Garrett County Medical Society, November 3, Drs. Walter T. Harrison, Washington, D. C., spoke on diphtheria immunization, and Karl Winfield Ney, New York, the idiopathic epilepsies.——Dr. Allen W. Freeman, Baltimore, spoke before the Howard County Medical Society, recently, on "The Future of Rural Medical Practice."

MASSACHUSETTS

Society News.—Speakers at the fifth annual meeting of the New England Obstetrical and Gynecological Society, November 22, included Drs. Frank A. Pemberton, Boston, on "Cancer of the Cervix—Prevention and Treatment"; Stewart H. Clifford, Boston, "Diseases of New-Born in Early Days of Life," and Herbert B. Nelson, Boston, "Analgesia in Labor."——Dr. Edward D. Churchill, Boston, among others, spoke before the Norfolk District Medical Society in Roxbury, November 28, on "Surgical Treatment of Empyema."

Personal.—Dr. M. V. Govindaswamy, delegated by the Mysore government (India) to make a special study of American psychiatry, is now serving as clinical assistant at the Worcester State Hospital, collaborating in the research activities. For the past two years Dr. Govindaswamy has served as clinical assistant at the Bangalore Mental Hospital.——Dr. Charles H. Lawrence, Jr., has resigned as assistant professor of endocrinology at Boston University Medical School.——Dr. Frederick L. Bogan, Boston, was appointed superintendent of the Sanatorium Division, Boston City Hospital, November 24, succeeding the late Dr. John F. O'Brien.

MICHIGAN

Meeting on Medical Economics.—A special meeting of the Wayne County Medical Society, December 20, was devoted to medical economics, with discussions of the Federal Emergency Relief Administration and the Civil Works Administration as concerns physicians, Michigan poor relief laws, and the doctor's situation in relation to them; the abuse of free and part pay clinics, and the state hospital at Ann Arbor. Mayor John W. Smith suggested that the unemployed be given health examinations by their private physicians so that each man may be in good physical condition when he is called back to work. This plan was also urged for all employees under the Civil Works Administration, because an examination at this time would protect the government against malingerers of the future, it was stated. Plans to correct certain abuses were registered and a permanent clinics committee appointed to execute them. The society will hold a "rally" on tuberculosis, January 22. Drs. Henry C. Sweany, Chicago, and Bruce C. Lockwood will discuss "Pathogenesis and Symptomatology of Childhood Tuberculosis." Henry F. Vaughan, Dr.P.H., commissioner of health of Detroit, will speak on "Medical Participation."

MINNESOTA

Society News.—Speakers before the Hennepin County Medical Society, December 27, were Drs. Jennings C. Litzenberg and Claude J. Ehrenberg, Minneapolis, on endocrine control of menstruation and dysmenorrhea, respectively.——The Minnesota Academy of Medicine was addressed, December 13, by Drs. Halbert L. Dunn and Martin Nordland on "Practical Experiments in What Actually Constitutes a Good Clinical Record" and "Diagnosis and Treatment of Malignant Tumors of the Thyroid Gland," respectively.——Dr. Earl E. Carpenter, Superior, was elected president of the Interurban Academy of Medicine, November 15, whose membership is made up of Duluth and Superior, Wis., physicians. Dr. Frank J. Hirschboeck, Duluth, is the retiring president.

MISSISSIPPI

Program of Malaria Control.—A state-wide malaria control and sanitation program will be carried on in Mississippi over a period of two and one-half months, newspapers reported, November 30. It will be handled as a federal works project instead of an undertaking of the state Civil Works Administration. Dr. Felix J. Underwood, state health officer, is supervisor of the program, and Dr. George E. Riley, chief of the malaria control division, will direct the malaria projects.

MISSOURI

Personal.—Dr. John C. Morfit was recently elected president of the St. Louis Medical Society.——Dr. Paul F. Stookey has been appointed epidemiologist of the Kansas City Health Department.

Kansas City Academy Programs.—The remaining lectures in the series of seven which comprise the 1933-1934 season of the Kansas City Academy of Medicine are as follows:

Dr. William T. Peyton, director, cancer clinic, University of Minnesota: Advancement in Diagnosis and Treatment of Malignant Disease, January 10.

Dr. Ralph S. Muckenfuss, assistant professor of medicine, Washington University School of Medicine, St. Louis: Practical Clinical and Therapeutic Problems as Related to the Study of Virus Disease.

Dr. Charles A. Doan, professor of medicine and medical research, Ohio State University College of Medicine: Clinical Implications of Experimental Hematology.

Dr. Loyal Davis, professor of surgery, Northwestern University School of Medicine, Chicago: Clinical Application of the Newer Discoveries in the Field of Neurological Surgery.

Other lecturers in the series were Drs. Albert M. Snell, Rochester, Minn., on "Differential Diagnosis of Conditions Associated with Jaundice"; Richard H. Jaffe, Chicago, "Endothelial Reticular System: Its Clinical and Pathological Relationships," and Dr. Robert T. Frank, New York, "Clinical Application of Newer Discoveries in the Field of Endocrinology."

NEBRASKA

Society News.—Dr. Walter Lawrence Bierring, Des Moines, Iowa, President-Elect, American Medical Association, delivered the principal address at the annual banquet of the Omaha-Douglas County Medical Society, December 12, on "Historical Sequence in Medical Events."——Drs. Thomas L. Houlton and Abram E. Bennett, Omaha, addressed the Otoe County Medical Society, Syracuse, December 11, on "Head Injuries and Their Immediate Treatment" and "Post-Traumatic Neurological Syndromes," respectively.——Speakers at the January meeting of the Lancaster County Medical Society, Lincoln, will be Drs. Miles J. Breuer, on "The Psychic Factor in the Etiology of Tuberculosis," and Ruth A. Warner and Grace Loveland, "A Satisfactory Technic for Early Pregnancy Tests." Dr. Newell C. Gilbert, Chicago, addressed the society, Lincoln, December 5, on heart disease.

NEW JERSEY

Award to Dr. Theobald Smith.—The Copley Medal of the Royal Society of London has been awarded to Dr. Theobald Smith, director emeritus of the department of animal pathology, Rockefeller Institute for Medical Research, Princeton, in recognition of his research on diseases of man and animals, notably his work in establishment of the theory of insect transmission of diseases.

NEW MEXICO

Typhoid in Taos County.—Sixty-two cases of typhoid occurred in twenty-nine families in two Spanish American communities near Taos during the early fall, according to the New Mexico *Health Officer* for November. Several possible sources for the epidemic were unearthed by Dr. C. H. Douthirt, who made an investigation for the state department of health, but none were definitely proved. Both Ranchos de Taos and

Llano are on an irrigation ditch from which many persons take their drinking water. The few wells in the area are dug wells open to surface drainage. Samples of water from the ditch were negative for B. coli, but water from four wells was positive. Twenty-five cases were definitely the result of direct contact with other cases in the same house; others of visits to relatives ill with the disease. Several patients had attended "velorios," gatherings at the homes of persons who have just died. On these occasions friends and neighbors spend the night, eating a midnight supper and breakfast in the home. Because of the distance from the state laboratory at Santa Fe, efforts to identify a carrier through laboratory examination were unsuccessful. Several deaths occurred. Some cases remained to be investigated. About 600 persons in the two communities received complete typhoid inoculations.

NEW YORK

Hospital News.—Mr. J. Ward Thompson, superintendent of Rochester Municipal Hospital for thirty years, died, October 27.——Contracts amounting to $882,486 have been awarded for the construction of a state hospital for tuberculosis at Mount Morris.——A tumor clinic was opened in November at St. Joseph's Hospital, Elmira, following a suggestion from authorities of the State Institute for Malignant Diseases at Buffalo, as a means of relieving overcrowding at the Buffalo institution. The clinic will be open one hour a week at first.

New York City

Personal.—Dr. Joseph Eastman Sheehan has been made a member of the French Surgical Society.——Dr. Simon Tannenbaum was the guest of honor at a testimonial dinner at Beth David Hospital, December 17, on his retirement as superintendent of the hospital. He will become medical director of Sydenham Hospital.——Dr. William Browning was the guest of honor at a meeting of the Medical Society of the County of Kings, November 21, in recognition of his services in building up the society's library. Drs. James P. Warbasse and Frederick Tilney paid tribute to Dr. Browning, who was guest of honor at a dinner at the Montauk Club before the meeting.

Society News.—Dr. Howard Lilienthal, among others, addressed the first fall meeting of the International and Spanish Speaking Association of Physicians, Dentists and Pharmacists, November 17, on "Dangers of Cerebral Embolism in Thoracic Procedures."—— Dr. David Riesman, Philadelphia, delivered the anniversary discourse of the Medical Society of the County of New York, December 18, on "Medieval Universities."—— Dr. Grant P. Pennoyer, New York, addressed the New York Surgical Society, December 13, on treatment of varicose veins and ulcers.——Dr. William Seaman Bainbridge addressed the Society of Medical Jurisprudence, December 11, on "The Rôle of Trauma in the Production of Cancer." This society celebrated its fiftieth anniversary, December 16.

OHIO

Public Health Lectures.—The Academy of Medicine of Cleveland and the Albert Fairchild Holden Foundation of Western Reserve University are sponsoring jointly the fourth annual series of public health lectures. Dr. Howard T. Karsner delivered the first lecture on "The Rôle of Germs in Modern Life," December 10. The second will be given by Dr. William Evans Bruner, January 14, on "Care of the Eyes in Youth and Age" and the third, February 18, by Dr. Harold N. Cole, on "The Skin in Health and Disease."

Appointments at Cincinnati.—Dr. Clarence King has been appointed professor and head of the department of ophthalmology at the University of Cincinnati College of Medicine, to succeed Dr. Victor Ray, who has been made professor emeritus. Dr. Gordon F. McKim, professor of urology since 1917, was made professor of surgery and head of the urological division to succeed Dr. E. O. Smith, who resigned because of illness. Dr. Smith was also made professor emeritus. To succeed the late Dr. Charles L. Bonifield, Dr. Frank M. Coopock has been appointed professor of surgery in the gynecologic division.

Society News.—Dr. George E. Follansbee, Cleveland, chairman, Judicial Council, American Medical Association, was the principal speaker at a meeting of the Eighth District Medical Society, in Cambridge, November 1; his subject was "Is Medicine a Profession or a Trade?"——Dr. George T. O'Byrne, Lima, addressed the Van Wert County Medical Society, November 7, on "Feeding of Premature Infants, with Special Reference to Copper and Iron."——Dr. Max M. Zinninger, Cincinnati, addressed the Stark County Medical Society, Alliance, November 14, on "Surgical Treatment of Acute Abdominal Emergencies."——Drs. George T. Harding, Jr., and George T. Harding III, Columbus, addressed the Tuscarawas County Medical Society, New Philadelphia, November 9, on "Present-Day Conceptions of Mental Disease."——Dr. George I. Nelson, Columbus, addressed the Crawford County Medical Society, Bucyrus, December 4, on cardiovascular disease.

PENNSYLVANIA

Hospital News.—The Robert Packer Hospital, Sayre, has obtained a loan and grant of $425,000 from the Public Works Administration, for use in completion of a seven story brick, fireproof hospital with a two story brick extension.——The Hospital Association of Pennsylvania has launched a campaign for exemption of hospitals from the state's new alcohol taxes.——St. Joseph's Hospital, Lancaster, recently celebrated its fiftieth anniversary.

Society News.—Dr. George W. Grier, Pittsburgh, addressed the Lawrence County Medical Society, December 7, on "Radium Treatment of Malignancy."—— Dr. Thomas E. Mendenhall, Johnstown, delivered an address on "Endocrine Secretions" before the Somerset County Medical Society, Somerset, November 21.——Among speakers before the Clearfield County Medical Society at the Philipsburg State Hospital, November 23, were Drs. James D. Doyle, Grassflat, on "Control of Complications Arising in Syphilis"; George A. Ricketts, Osceola Mills, "Spontaneous Subarachnoid Hemorrhage," and Lester Luxenberg, "Metallic Poisoning."——A symposium on appendicitis was on the program of the Dauphin County Medical Society, Harrisburg, December 5, presented by Drs. Herbert F. Gross, John A. Fritchey, Earle R. Whipple and Frank F. D. Reckord.——The Allegheny County Medical Society in cooperation with the Pittsburgh Child Guidance Center sponsored a public lecture in Pittsburgh, December 7, on "Mental Hygiene Problems of Today and Tomorrow," by Dr. Bernard Glueck, New York.——The Montour County Medical Society sponsored a symposium on goiter at the Geisinger Memorial Hospital, Danville, December 1. An operative clinic was held in the morning and a scientific program in the afternoon, with Drs. David Marine, New York, Frank H. Lahey, Boston, and William F. Rienhoff, Jr., Baltimore. Dr. Harold L. Foss, Danville, was chairman of the program.——Dr. Temple S. Fay, Philadelphia, addressed the Cambria County Medical Society, Johnstown, November 9, on "Dehydration and Its Application."——Dr. Walter Estell Lee, Philadelphia, addressed the Delaware County Medical Society in Chester, December 14, on "Postoperative Pneumonia."

Philadelphia

Medical Economics Program.—The meeting of the Philadelphia County Medical Society, January 10, will be devoted to discussions of medical economics. Hon. J. Hampton Moore, mayor of Philadelphia, will give an address on "The Municipality and the Medical Profession" and the following physicians will speak: Drs. Frederic E. Elliott, Brooklyn, chairman of the committee on economics of the Medical Society of the State of New York, on "Adjustment of Medicine to the Newer Economic Philosophy"; Seth A. Brumm, president-elect, Philadelphia County Medical Society, "The Activities of the Commission on Medical Economics in Retrospect," and Francis Ashley Faught, chairman, "Activities of the Commission on Medical Economics in Prospect."

SOUTH CAROLINA

Society News.—Dr. Madison Hines Roberts, Atlanta, addressed the Greenville County Medical Society, recently, on problems of the new-born.——Dr. William Egleston, Hartsville, president, Medical Society of South Carolina, among others, addressed the Fourth District Medical Association at Spartanburg recently, on functions of the state board of health.——The Third District Medical Association held a meeting, October 5, at which speakers included Drs. Ernest W. Carpenter, Greenville, on nasal sinus problems, and George R. Wilkinson, Greenville, nonsyphilitic aortitis.

TENNESSEE

Hospital News.—Drs. Dean Lewis, Baltimore, President, American Medical Association, and James B. McElroy, Memphis, were guest speakers at an institute for physicians at Rutherford Hospital, Murfreesboro, November 27-28, under the auspices of the Commonwealth Fund. Dr. Lewis spoke on tumors of bone, fractures, lesions of the breast and diseases of the thyroid, and Dr. McElroy on malaria, anemias and Bright's disease.——Wheat's Hospital, Lewisburg, was burned, November 13, with a loss of about $40,000.

Society News.—Dr. Daugh W. Smith presented a review of 292 cases of incomplete abortion at a meeting of the Nashville Academy of Medicine, December 19. Dr. Merrill Moore, Boston, addressed the academy, December 9, on acute syphilitic meningitis.——Drs. Horace B. Cupp and Edward T. West addressed the Washington County Medical Society, Johnson City, December 7, on "The Rôle of Fluid in Surgery" and "Surgery of the Biliary Tract," respectively.——Dr. Martin H. Fischer, Cincinnati, addressed the Gibson County Medical Society, Trenton, November 27, on diseases of the blood vessels. ——Dr. Robert B. Gaston, Lebanon, was elected president of the Middle Tennessee Medical Association at its semiannual meeting in Murfreesboro, November 23-24. The next session will be held in Springfield. Among the speakers was Dr. William D. Haggard, Nashville, who discussed appendicitis.

WASHINGTON

Society News.—Drs. William F. Patrick and Ivan M. Woolley, Portland, Ore., addressed the Cowlitz County Medical Society, October 11, at Cathlamet, on "Differential Diagnosis and Acute Diseases of Children" and "X-Ray Diagnosis," respectively. —— Dr. Siegfried F. Herrmann addressed the October meeting of the Pierce County Medical Society, Tacoma, October 10, on "Anomalies of the Gallbladder."——Drs. Samuel L. Caldbick, Everett, and Elijah C. Leach, Arlington, addressed the Snohomish County Medical Society, Everett, October 3, on "Fractures in the Region of the Elbow Joint" and "Nonunion of Fractures," respectively.——Dr. James Marr Bisaillon, Portland, Ore., addressed the Walla Walla Valley Medical Society, October 12, in Walla Walla, on "Differential Diagnosis of Postoperative Lung Complications" and Drs. James T. Rooks, Jesse W. Ingram and Carl J. Johannesson, Walla Walla, on "Pulsion Diverticulum of the Pharynx."——Drs. David Metheny and Joel W. Baker, Seattle, addressed the Yakima County Medical Society, Yakima, October 9, on "Intra-abdominal Repair of Inguinal Hernia" and "Retroperitoneal Approach to Subphrenic Abscess," respectively.——Dr. James M. Bowers, Seattle, presented a clinical study of gastric ulcers at a meeting of the King County Medical Society, Seattle, November 6; the paper was discussed by Dr. Andrew B. Rivers, Rochester, Minn., who also conducted a clinic at Harborview Hospital in the afternoon preceding the meeting. C. Rufus Rorem, Ph.D., Chicago, addressed a special meeting, November 17, on "Paying for Medical Care," and Drs. Arnold W. Hackfield and Donald V. Trueblood, Seattle, spoke, November 20, on "Interpretation and Treatment of Functional Symptoms" and "Radiation Therapy or Surgery for Cancer," respectively. —— The Lewis County Medical Society gave a banquet in Chehalis, November 13, in honor of its pioneer members: Drs. John T. Coleman, James M. Sleicher, Emmogene P. Sherman, Chehalis, and William Botzer, Mossyrock.

WEST VIRGINIA

Antidiphtheria Campaign.—The Kanawha Medical Society and the health department of Charleston conducted an intensive campaign of diphtheria immunization, November 9-30. Henry F. Vaughan, Dr.P.H., health commissioner of Detroit, visited Charleston, November 7, to assist local authorities in planning the campaign, which was carried out according to the Detroit plan, in which immunization is done in the offices of private physicians. Dr. Vaughan also made a formal address on this subject before physicians of the city. Originally planned for only a few days, the campaign was continued for the rest of the month. During the first intensive drive, 2,210 children were immunized in physicians' offices. Toxoid was furnished by the state health department. An unusual number of cases in the city led Dr. Hugh B. Robins, city health officer, to inaugurate the plan.

WISCONSIN

Hospital Anniversaries.—The Marinette and Menominee Hospital, Marinette, celebrated the fiftieth anniversary of its founding, November 9, with a reception, at which Dr. Clarence H. Boren reviewed the history of the hospital and the town of Marinette. The hospital staff held an informal meeting in honor of Mr. John E. Boren, superintendent, who has been affiliated with the institution for forty-nine years, and of Drs. Maurice D. Bird, Alexander T. Nadeau and Henry F. Schroeder, who have been associated with the hospital for twenty-five years. The hospital was founded by the late Dr. Horace Mann.——The Milwaukee Hospital, Milwaukee, celebrated the seventieth anniversary of its founding, November 5-6. A tablet was unveiled honoring the three chiefs of staff who preceded the present chief, Dr. Curtis A. Evans; they were Drs. Nicholas Senn, William Mackie and Harry A. Sifton. Speakers included Drs. Stanley J. Seeger, president of the State Medical Society of Wisconsin, and Robert Sayle, a member of the hospital staff for twenty-five years. There were also dinners for the nursing staff and for the medical staff, auxiliary board and interns' association.

WYOMING

Banquet in Honor of Dr. Conway.—The Laramie County Medical Society gave a banquet, November 15, in honor of Dr. John H. Conway, Cheyenne, who retired from active practice in October after forty years' service. Dr. Galen A. Fox, president of the society, presided and Dr. George P. Johnston paid tribute to Dr. Conway.

PUERTO RICO

Bust of Dr. Ashford.—Special ceremonies in the School of Tropical Medicine of the University of Puerto Rico, San Juan, December 16, marked the unveiling of a bronze bust of Dr. Bailey K. Ashford, recently retired as a colonel of the medical corps, U. S. Army. Hon. Benjamin J. Horton, acting governor of Puerto Rico, presented the bust to the school of medicine, and George W. Bachman, Ph.D., director, made the speech of acceptance. Other speakers were Carlos Chardón, chancellor of the University of Puerto Rico, and Dr. Rafael Bernabe, president, Medical Association of Puerto Rico. The casting of the bronze bust was unanimously approved by the legislature to recognize Dr. Ashford as founder of the School of Tropical Medicine and as initiator of the first campaign against hookworm disease in America (THE JOURNAL, December 16, p. 1976).

GENERAL

Change in Status of Licensure.—The New York State Board of Medical Examiners reports the following action taken in September:

License of Dr. William J. Ryan, Oakfield, N. Y., revoked by the board of regents on the ground that he had been convicted of a felony; namely, criminal abortion.

The state medical board of Ohio reports the following action taken October 3:

License of Dr. Johanna A. C. Roth, Columbus, suspended for six months because of her conviction on a charge of violating the federal narcotic law.

News of Epidemics.—The Civilian Conservation Corps camp at Elk Grove, Pa., was placed under quarantine, December 7, when four members of the corps developed diphtheria. ——Schools in ten communities in one section of Muskingum County, Ohio, were closed, December 4, to stop the spread of scarlet fever; they were to remain closed until after the holidays.——Churches, schools and the public library were closed in Vienna, Ill., December 19, in an effort to prevent spread of scarlet fever.——An epidemic of mumps was reported to have affected one eighth of the population of 400 in the village of Pearl City, Ill., December 20. The public school was closed.

CANADA

Society News.—Dr. Harold Beckwith Whitehouse, professor of gynecology and obstetrics, University of Birmingham, England, addressed the Toronto Academy of Medicine, October 14, on the menopause. Dr. Paul Dudley White, Boston, spoke, November 7, on "The History of the Development of Our Knowledge of Heart Disease."

New Minister of Public Health.—Dr. Frank Roy Davis, Bridgewater, was recently elected to the provincial legislature of Nova Scotia as minister of public health, succeeding Dr. George H. Murphy, Halifax. Dr. Davis, a graduate of Dalhousie University, has been medical officer of health of Lunenburg County since 1923 and has been on the surgical staff of Memorial Hospital, Bridgewater, for fifteen years. He also served as mayor of Bridgewater for four years.

University News.—*Canada Lancet and Practitioner* devoted its December issue to the class of 1892 of the University of Toronto Faculty of Medicine. Of fifty-four graduates, six remain in Toronto, fourteen are in Ontario, one is in Manitoba, fourteen live in the United States and twenty have died. One member of the class, Dr. Herbert A. Bruce, is lieutenant governor of Ontario.——A medallion of bronze commemorating the late Dr. Alexander S. Monro, president of the Canadian Medical Association in 1931, was recently unveiled at the University of British Columbia. Dr. Monro bequeathed a substantial fund to the university for medical education when a medical school is established at the university.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Dec. 9, 1933.

The Radium Treatment of Cancer

The fourth annual report of the National Radium Trust and Radium Commission deals with the work of the past year and also summarizes the progress made in the four years since the commission came into being. There is now a network of seventeen fully equipped radium centers all over the country, and the organization, as originally planned, can be regarded as complete. The commission controls 22 Gm. of radium, which is slightly in excess of the amount recommended by the committee of inquiry in 1929 as sufficient for the medical purposes of the country. The present report states that five years must elapse before an answer can be given to the question as to how much value can be attached to the radium treatment of cancer. Hence it is not possible as yet to see what effect the "national" policy is having on the cancer problem. Meanwhile, good work is being done in various directions, despite the discontinuance of the 4 Gm. radium "bomb." The commission has been developing a 1 Gm. unit treatment at three London hospitals. It is found that this type of massive radiation produces no serious or unforeseen constitutional disturbances with a maximum exposure of six hours a day and is likewise free from danger for the technical and nursing staff. The commission is leaving the problem of the large radium "bomb" to the newly constituted Radium Beam Therapy Research Board. Another valuable part of the commission's scheme is the postgraduate school of radiotherapy at Mount Vernon Hospital and the Radium Institute. More than 300 persons have now received instruction there. During the year a register of statistics to the commission, Mr. R. W. Raven, F.R.C.S., has been appointed, and the summary cards supplied by the centers are being used for the compilation of yearly statistics. It is to this department that the greatest interest will be attached, for by its work the value of radium treatment will be determined.

The Toll of the Roads

The death toll of the roads remains a serious problem. In an inquest at Birmingham on a woman aged 68, killed in a street accident, the coroner said that in all these inquiries it was impressed on him that old persons did not stand a chance if they failed. In the main roads carrying fast traffic, people should be given a reasonable oasis of safety for crossing. If necessary, traffic must be cut into sections, as was done in continental cities. They had surely got beyond the stage when, because an unfortunate person on foot did something wrong, he must lose his life. There was an onus on drivers in busy thoroughfares to keep a reasonable watch in order to combat some failure on the part of pedestrians. At Preston during "the safety week," nineteen persons were injured—twice as many as last year. The chief constable's comment was: "It is an unfortunate coincidence, but our efforts were directed to children, not adults. Adult pedestrians are past redemption."

The total number of persons killed in road accidents in Great Britain during 1930 was 7,305; during 1931 it was 6,691, and during 1932, 6,667. During the first six months of 1933 the number was 3,061, as a result of 2,998 accidents. An analysis was made of the fatal accidents according to the hours of the day. During the early morning hours, when there is little traffic on the roads, the percentage is small (0.4). It rises to a small peak between 7 and 9 a. m. (3.4), drops between 9 and 10 (2.6) and then increases, rising to a further peak between noon and 1 p. m. (7.0). It then declines but rises again after 3 and reaches its highest point between 5 and 6 (9.4). It then gradually decreases but reaches a further peak between 10 and 11 (7.3). These peaks depend on variations in the volume of traffic, both pedestrian and vehicular. Thus there are peaks at the time many people go to work, during the luncheon hours, and when a large number return from work. Of the persons killed in the first six months of 1933, 1,581 were pedestrians, of whom 857 were killed crossing roads, and of these 224 were passing behind or in front of a stationary vehicle; 314 pedestrians were killed not when crossing the road but when running into the roadway; 46 were killed on footpaths, 71 on a refuge; 84 were killed when walking along roads. Of the pedestrians killed while walking on the carriage way, 66 were walking in the same direction as the traffic and 18 against it. Where no footway is available, the highway code recommends pedestrians to walk on the right of the carriage way, so as to face the oncoming traffic.

THE CAUSES

A long table gives all the causes of the fatal accidents assigned by the chief constables. Only 265 out of 2,963 accidents analyzed gave excessive speed as a contributory cause. Inattention on the part of a driver was given as a contributory cause in 139 accidents. Pedal cyclists gave a high number of cases and in practically all the cyclist was the victim. Of the contributory causes attributable to pedestrians, "running into the roadway" was the most frequent and, next, "pedestrian walking or running from behind a vehicle without due care." In 242 accidents, "pedestrian apparently becoming confused or hesitating in traffic" is given as a contributory cause. Apart from mechanical defects, the most important cause contributed by vehicles was inadequate front lighting (thirty-two accidents). Dazzling headlights contributed to twenty-nine accidents. A frequent contributory cause was obscuration of the views of drivers at corners or bends.

PARIS

(From Our Regular Correspondent)

Nov. 15, 1933.

The Congress of Urology

The thirty-third congress of the Association française d'urologie was held at the Faculté de médecine, under the chairmanship of Dr. Bernasconi of Algiers. The topic for discussion was "Methods Other Than Prostatectomy for the Treatment of Hypertrophy of the Prostate." The preliminary papers were presented by Drs. Bernard Frey and Raymond Dosset of Paris. Medical treatment by the injection of pepsin-procaine into the prostate, the administration of testicular hormones, and the subcutaneous injection of the male hormone are methods that are being tried out. The resection of the vasa deferentia has been abandoned in France. Roentgenotherapy and radium therapy are of questionable value, and they are dangerous in case of infection. Since they are always combined with the use of sounds and with lavage, it is difficult to determine just what their influence has been. They are permissible in beginning cases without retention, and in the congestive types, but are contraindicated in aged and infected patients and in those who have large adenomas. There remain the resection methods performed, with the aid of endoscopy, by the transvesical or the urethral route. The authors considered these methods, comparing them with the results of classic prostatectomy. Partial transvesical resections have advocates in France (Legueu, Heitz-Boyer, Martin-Laval) in cases in which the ordinary operation would be dangerous on account of the size of the tumor, the risk of hemorrhage or the general condition of the patient. Resections by the intra-urethral route and electrocoagulation give, in general, good immediate results.

This is, however, a delicate operation for the surgeon who has had wide experience with its technic, and it is contraindicated in cases presenting very large or bleeding prostates in which neoplastic degeneration is suspected. The statistics of American surgeons are impressive.

A long discussion arose between the members of the congress concerning their results. Professor Marion prefers prostatectomy in all cases in which the condition of the patient justifies the operation and also in cases in which other methods have proved ineffective. In patients unable to withstand prostatectomy, and in patients strong enough to endure the operation but who have only small adenomas, one can attempt destruction of these by conservative means. The same methods may be tried to destroy larger adenomas in persons who cannot withstand transvesical prostatectomy. Radium should be reserved for weak patients who could not endure an operation. Dr. Luys defended his forage operation on the prostate and presented statistics to prove its benign nature. But the endoscopic methods encountered opponents, who contended that they were incomplete and did not always prevent infection, hemorrhage or even death. Blanc of Bordeaux, Guisy of Athens, Gayet and Phélip (Lyons) and Chauvin of Marseilles reported a few successful outcomes in very simple cases; but they expressed the opinion that prostatectomy is still the only effective operation with which to combat adenoma of the prostate, especially since advances in technic have reduced the risk of operation. That is the view also of such eminent urologists of Paris as Papin and Pasteau. In fact, Pasteau rejects every other intervention as illusory and dangerous. Many of the advocates of the various substitutes for prostatectomy, with the exception of Luys, resort to endoscopic methods only in special cases.

Numerous further communications dealing with diverse subjects were presented. Phélip of Lyons cited several cases of urinary infection of dental origin, transmitted by the blood stream. Pasteau reported a case of pharyngeal origin. Widbolz of Bern stated that he had secured excellent results in nontuberculous aseptic pyuria by means of intravenous injections of neoarsphenamine in doses of 0.0015 Gm. Mr. Pillet reported some curious observations to the effect that, in alkaline urine, the formation of phosphatic, ammoniacomagnesic calculi is facilitated by pyrexia, a rise of from 1 to 3 degrees in temperature being sufficient to precipitate these crystals when all the elements are combined. Mr. Barbellion called attention to the following test to discover whether a patient has recovered from gonorrhea: After the imbibing of an abundance of beer, massage of the prostate, not followed by lavage or urination within five hours; examination of the urethral secretion for the presence of gonococci. In positive cases, especially if the patient has engaged in coitus, the urine will be found to contain gonococci. In negative cases gonococci will not be found.

Jules Janet and Debains discussed gonococcal autovaccines and expressed a preference for those in which the gonococcus has been killed at the lowest temperature possible, in order not to change its biologic properties. They are superior to stock vaccines because they contain gonococci of the desired strain, and fresh specimens. Jeanbrau and Truc (Montpellier) reported a case of complete retention of urine in a woman for thirteen months, which was immediately cured by the Cotte operation, consisting in resection of the presacral nerve. Dr. Lowsley of New York gave an exposition of three of his procedures in renal surgery. He sutures the wounds of the kidney in nephrotomy with a ribbon of catgut, which envelops the organ and which is held in place by passing it, cut into several strips, into the fibrous capsule. He arrests hemorrhage of the parenchyma by introducing fatty tissue into the wound, which he regards as the best type of hemostatic. He performs nephropexy by fastening the kidney by two strips of chromic catgut, one at each of its poles, the one being attached to the twelfth rib and the other to the quadratus lumborum muscle.

Dr. Harvey Cushing Honored

The ceremonies in connection with the formal reopening of the University of Paris, this year, were attended by the president of the republic. The several scientists who were accorded the title of doctor honoris causa were all present, each wearing the garb of his own university. Dr. Cesar Vivante, professor of law at the University of Rome; Professor Levi-Civita of the faculty of sciences, University of Rome; Mr. Puig y Cadalfach, president of the Catalan Institute of Barcelona; Professor Van Itallie of the University of Leyden; Prof. Franz Volhard of the University of Frankfort, and Dr. Harvey Cushing of Yale University, on whom special honors were bestowed. Professor Roussy, dean of the Faculté de médecine, made this declaration: "I render public homage not only to one of the greatest surgeons of the United States of America but also to the man whose work in anatomy, physiology and clinical surgery has brought great progress to modern neurology and to the ingenious inventor whose new forms of technic have made it possible, during the past thirty years or more, to save thousands of lives." Then, after enumerating the chief works of this master of neurology and rendering homage to the surgeon and teacher, Professor Roussy concluded with these words: "Georges Clemenceau, then minister of war and president of the cabinet, in recognition of your valuable aid given to the ambulance companies, during the war, in the region of Neufchâteau, desired, at the time of your departure from France, to give a testimonial of his esteem and gratitude. His gift was his doctor's thesis in medicine, submitted in 1865, which is a very rare booklet. This esteem, this gratitude, and this admiration, the University of Paris and the medical profession of France are happy to take this occasion to endorse."

BERLIN

(From Our Regular Correspondent)

Nov. 13, 1933.

Anemia Due to Goat's Milk

Professor Rominger, director of the university children's clinic in Kiel, has begun a research on the pathogenesis and therapy of anemia due to the use of goat's milk. On the basis of comprehensive studies on metabolism in healthy and sick children who were nourished with goat's milk, and observations in animal experiments, he discussed the question as to whether anemia due to goat's milk is the result of a trophotoxic or a trophopenic injury. Clinical observations show that it is at least improbable that goat's milk as such has any toxic qualities. Feeding experiments on young growing white rats led to the conclusion that an exclusive diet of cow's milk produces an anemia of the chlorosis type (hypochromic anemia), which is evidently due to a lack of iron, since it can be both prevented and cured by the administration of iron. An exclusive diet of goat's milk produces in very young white rats an anemia of the pernicious type (hyperchromic anemia). This experimental hyperchromic goat milk anemia cannot be cured solely by the administration of iron; nor is it due to a lack of vitamin C. Furthermore, it can neither be produced nor exacerbated by the administration of unsaturated volatile fatty acids of goat's milk. It can, however, be prevented and cured by the injection of liver extracts. It is a complex deficiency disease, in which the factor that counteracts any tendency to perniciousness —namely, the so-called extrinsic factor—is absent, and likewise iron. The good effects of a combined liver extract and iron therapy were observed by Rominger. Within four weeks, therapeutic results could be secured such as were obtained with the former therapy, even along with the application of

blood transfusions, usually only after several months. According to these observations, arsenic, artificial heliotherapy and extirpation of the spleen are no longer indicated. From the standpoint of prophylaxis, the use of goat's milk without the addition of liver and iron must be avoided; but if these additions are made, there is no objection to goat's milk in the diet of infants. It may be mentioned that goat's milk contains more copper than other kinds of milk.

Adopt Policy of Free Choice of Physician

Previous letters have dealt with the reorganization of the federal krankenkassen system (THE JOURNAL, November 18, p. 1652). At last the controversy that existed in Berlin between the municipal administration and the Gross-Berliner Aerztebund, with reference to the proper care to be given to the so-called welfare aid unemployed, has been settled. To this class belong those who, since they have no income, pay no dues to the krankenkassen. The municipality itself must provide for them. Until recently, members of this group in some districts of the city had to apply, in case of illness, to a certain "welfare physician," who devoted only part time to this service. This arrangement did not result in very confidential relations between physician and patient. Furthermore, the number of part time "welfare physicians" was so small that often unpleasant situations occurred owing to the crowded conditions prevailing during consultation hours. In other districts, those in need of aid had a free choice of physician, but the compensation of the physicians was very small. Both parties, therefore, failed to be satisfied with this system, and the medical profession of Berlin carried on a campaign for years to secure for such patients and for themselves something more satisfactory. Now, the system of part time physicians has been abolished in Berlin. The physicians now receive a fixed amount annually for each patient who, over an extended period of time, belongs to this group, while intermittent care given certain patients is paid for according to service rendered. As a result of a new system in which the vertrauensärzte, or confidential physicians, of the krankenkassen, play an important part, there seems to be some expectation that the superfluous use of medicines will be checked. For this purpose, a central prescription control center has been established at the municipal bureau of health. Domiciliary treatment will be restored to its former position, to which it is entitled. Thus, the old demand of the physicians for a free choice of physician by patients has been set up in Berlin, at least as far as the physicians admitted to panel practice are concerned. In view of the financial condition of Berlin, it is impossible to satisfy all the financial desires of the physicians.

In Hamburg, the waiting room problem has been taken up by the Hamburg "chamber of physicians," which has declared that it is absolutely inconsistent with the idea of popular sovereignty to make, in a physician's waiting room, any distinction with respect to patients, as to whether they are "welfare patients," krankenkasse patients or private patients. Hence, dating from this announcement, special consultation hours for private patients, and the equipment of special waiting rooms for such patients, are prohibited.

The Berlin Academy for Graduate Training

Although, for decades, facilities for the training of domestic and foreign physicians have existed in the city, Berlin will open in January an academy for graduate medical training. The instructors, who must be teachers in the various specialties, will be selected by the mayor, with the aid of a scientific committee on instructors. The purpose will be to organize graduate medical training on a uniform basis and to afford an opportunity to general practitioners, specialists, assistant physicians in the municipal hospitals, and physicians in other communal welfare departments, to participate in courses and in practical activities. It is the plan to organize, for the benefit of physicions of Berlin and vicinity who have little leisure in the evenings, lectures and demonstrations covering one or two hours a week, for a period of from two to three months, in many different hospitals of Berlin. In addition there will be eight to fourteen day courses on selected subjects, with practical demonstrations. To give physicians the opportunity to do practical work from clinical points of view, whole-day clinical instruction courses with the chief emphasis on practice work will be held in the municipal hospitals, which, it is thought, will make for a better understanding between the general practitioner and the specialist.

Further Details on the Higher Institutions of Learning

Reorganization of the higher institutions of learning (THE JOURNAL, Dec. 16, 1933, p. 1980) is proceeding in various directions.

The league of the German institutions of higher learning, the conference of German rectors, the federation of German university teachers, the Bavarian league of university teachers, and the society "The German State," have voluntarily combined, with a view to promoting a federal organization of all German institutions of higher learning and of the teaching personnel of such institutions. The new organization, under the supervision of the federal ministry of the interior, will protect the cultural importance of the German institutions, also in relation to foreign countries, and will cooperate in renovating the German system of higher instruction in agreement with the national-socialist world-view and in the endeavor to make the universities an organic part of the German body politic and the national life. Prof. Herwart Fischer, ordinarius in legal medicine at the University of Würzburg, has been chosen as leader of the new organization.

After the beginning of the winter semester, the training school, which has assumed the task of giving the new type of students preliminary training in statecraft, will reopen. The objective of this political training is the acquisition of knowledge that will fit the student to play a prominent part in national politics. The University of Berlin student body has published a work schedule and study plan that illustrate the essentials of this new movement, the fachschaftsarbeit. According to this plan, this work is compulsory for all students of the second and third years. A special training of a wider scope has been prepared for the first year students. Those who have attended German universities three years are not required to participate in the fachschaftsarbeit but it is recommended that they do so. The work is not compulsory for women, but they will be admitted to the courses as volunteers.

Depending on whatever is their major subject, the students are divided into six different groups, or so-called fachschaften. The group interested in popular education will study conditions in eastern Germany, the minority problems of the last century, and German-Russian relations. The group interested in German law will study "The State" and the protection of races and of nationality in the penal code. In the group interested in political economy, the colonial director of Greater Berlin, of the national-socialist party, will speak on national-socialism and colonies. The theological group will discuss symbolics, or historical theology, and its significance for our day—particularly Luther, Melanchthon and Calvin. The medical group will study race problems and social problems. The group interested in the natural sciences will be divided into four subgroups: biologic, geographic, mathematicophysical and chemical. At the close of the semester, every student receives a certificate setting forth the work performed. The movement will have a special journal, called *Wissen und Dienst*, to be edited by the director of the Berlin circle of the German student federation.

Number of Health Insurance Societies in Germany

From the reports of the head insurance bureaus, it will be seen that at the close of the year 1932 there was a total of 6,638 krankenkassen; namely, 2,046 communal krankenkassen (ortskrankenkassen), 428 rural krankenkassen, 3,266 krankenkassen of industrial units (betriebskrankenkassen), and 798 krankenkassen of guilds (innungskrankenkassen). The last two categories show a reduction in membership, which has been further accentuated since the reorganization of the whole federal health insurance system.

Professor Magnus to Direct Surgical Clinic

The university surgical clinic in the Ziegelstrasse in Berlin (not the clinic in the Charité Hospital, which is under the direction of Professor Sauerbruch) had been closed (by the former government). The new government announced, several months ago, that this famous clinic (Professor Bier being the last incumbent) would be reopened. To this important post Prof. Richard Magnus, chief physician of the Bergmannsheil Hospital in Bochum, has been called. Magnus, who is 50 years old, is a pupil of Friedrich, König and Guleke. The hospital of which he has been a director is regarded as the largest hospital in Europe for patients who have suffered accidental injuries. Magnus's numerous publications deal chiefly with the treatment of fractures, war surgery and problems concerning joint infection.

Professor Siebeck Summoned to University of Berlin

The chair of internal medicine and the directorship of the first University Medical Clinic, formerly held by Professor His, had been vacant some time; but now Prof. Richard Siebeck, clinician of the University of Heidelberg, has been summoned to occupy the post. Volhard of Frankfort-on-Main recently rejected the offer, and, still earlier, Schittenhelm of Kiel was not inclined to move to Berlin. Siebeck is 50 years old. At the University of Heidelberg, he has been occupying the chair of his former teacher Krehl. His published writings deal chiefly with disturbances of the circulatory and respiratory organs, and with the kidneys and with the water balance.

JAPAN

(From Our Regular Correspondent)

Oct. 28, 1933.

Vaccination Against Typhoid

Typhoid vaccination has again become the subject of heated discussion in medical circles all over the country. Typhoid vaccination has been widely adopted in places exposed to this disease, and yet its absolute potency is never relied on. At a meeting of the Kitasato Research Institute, Dr. Kobayashi of the Keio Medical College recently criticized the value of typhoid vaccination. His paper provoked discussion in various circles throughout the country. His criticism was directed chiefly against the statistical reports of the metropolitan police board. He said that it is very difficult to form a conclusion on the potency of vaccination merely on the basis of statistical research for, in a sudden outbreak of typhoid, complete protection could not be expected.

Dr. Inokuchi, chief of the prevention bureau of the metropolitan police board, says that in the metropolis in the past eight years about 1,600,000 people have been inoculated almost every year. The percentage that contracted the disease among the inoculated has varied from 3.5 in 1925 gradually down to 0.67 in 1930. On the other hand, the death rate among the inoculated averaged 15 per cent, more or less, but among the noninoculated was almost 20 per cent every year. He insists that the smaller death rate must be attributed to the increase in the annual inoculations, which tends greatly to reinforce the potency of the immunization. He says that of late some people have been inclined to lessen the amount of vaccine used for fear of reactions, but even a smaller quantity and a less potent vaccine, if repeated every year, is a certain preventive. Where sanitation is so poor as in the capital, this inoculation should be considered an essential measure for the time being. Dr. Kajitsuka, dean of the military medical school, says that the army believes in vaccination, even if not in its absolute value, and if an improvement in the kinds of vaccine to be inoculated could be attained, a much greater effect might be realized. Statistically, the death rate in the army has been lowered through yearly inoculation. On the other hand, according to reports given by Dr. Kawaguchi, chief of the isolation hospital of Tokyo, hardly any difference could be recognized between the vaccinated typhoid patients and the nonvaccinated, at least in his hospital. Toxic conditions and nervous system complications seemed rather more severe among the inoculated, among whom the death rate was often higher. Of course, sometimes an inoculated person had a mild attack of typhoid. He therefore was bewildered as to the effect of the inoculation. Some discharged soldiers who had been inoculated while in the army, he says, contracted severe typhoid soon after their discharge. He doubts its essential effect.

Dr. Urabe, medical expert of Nagasaki, a seaport, reported in detail his investigations, saying that since 1926 the number of those who were inoculated had increased every year but that the number of cases of typhoid had increased or remained the same yearly.

In 1931 a sudden outbreak of typhoid took place there, and the rate was quite high. He concludes that the period of immunity is uncertain. He reported 146 cases occurring within one month after vaccination, sixty-six cases within two months, and forty-one cases within three months. Inoculation during an epidemic therefore seems to be of comparatively little use. He adds that a little vaccine should be given frequently rather than a great deal at one time. About 10 per cent of those vaccinated were obliged to go to bed on account of reactions. This was caused by negligence in the observation of the specific type of constitution of some people, and also by giving them too much vaccine. He continued that the great loss of money and of time, both by the public and by the municipal office, should be considered in view of the comparatively small value of vaccination. He earnestly longs for some better measure in typhoid prevention.

Dr. Tashiro, surgeon commander of the imperial navy, in opposition to the former opinion, said that he has every reason to believe that the period in which inoculation remains potent is about six months. In the navy every sailor is vaccinated twice a year. The reason typhoid may be contracted in the first month after vaccination he attributes to the fact that the immunizing bodies develop insufficiently during that period to be really potent. In Moji, another seaport, the typhoid cases were about five a month before general inoculation began all over the city, but in April of this year inoculation was given to about 40,000 persons (40 per cent of the whole population) and 4,948 persons were given vaccine orally. In May, thirteen cases, and in June, twenty cases suddenly broke out among those who took the vaccine orally, not among those inoculated.

On the contrary, in the city of Ito, near Tokyo, vaccination against typhoid has been regularly done since 1921, accompanied by improved sanitation necessary to annihilate typhoid. In 1921, 139 cases were reported before inoculation, but the number of cases has gradually and regularly decreased year by year. In 1932, only three cases were found. The city authorities and the physicians concerned are firm believers in the effectiveness of vaccination. On the whole, more statistical investigations must be reported to decide the question. Many believe that the absolute value of inoculation will be established sooner or later.

Free Medical Advice to Athletes

In the physical development research institute of Japan, attached to the educational department, an athletic medical consultation office has been opened. Any one who needs advice on physical training may have a medical examination free of charge. Sports and competitive games are prone to lead young people into some danger of overexertion. The office is in charge of Drs. Saito and Shiraishi, the former being the chief of its internal medicine bureau, the latter of the surgical section. From the first day it was open, many athletes and players, both amateur and professional, visited the office to be examined, for this sort of medical advice has long been desired.

Personals

Dr. K. Futaki has retired from Tokyo Imperial University, where he held the chair of epidemic diseases.

Dr. R. Arima, an authority on tuberculosis, was decorated by the Hungarian government especially for the donation of his tuberculosis vaccine AO, which he presented while he was staying in Hungary last year.

Chian Sagara (1830-1909) was the first president of the Tokyo Imperial University and the director of its medical department. He adopted German medicine in this country for the first time. The present site of the Tokyo Imperial University was chosen by him. But he fell a victim to slanderous tongues and was obliged to retire from his high position. His after-life was miserable and he was forgotten. On the proposal of prominent people, including the war minister, Marquis Okuma and Viscount Dr. Ishiguro, a monument will be erected to this benefactor of Japanese medicine.

Marriages

Byron Ludwig Steger to Miss Delene Elizabeth Lobdell, both of Huntington, Ind., at Wabash, November 15.

Thomas H. Tomlinson, Thomasville, N. C., to Miss Mary Sweeney of Baltimore, at Greensboro, November 16.

Kutcher Threepoot Klein to Mrs. Iva W. Lovell, both of Meridian, Miss., at Jackson, in November.

Charles Neil McBryde, Ames, Iowa, to Mrs. Virginia Abbey Swergard at Nashua, September 2.

John M. Renehan to Miss Helen O'Donnell, both of Ansonia, Conn., at Milford, November 6.

Harold D. Waltz, Denver, to Miss Eleanor Frances Bassett of New Orleans, November 29.

Thomas Robert Plumer, Trivoli, Ill., to Miss Helen Cornelius of Peoria, November 15.

William Winslow Wiedemann, Jr., to Miss Sue Amstutz, both of Toledo, Ohio, October 10.

Irvin William Wilkens, Indianapolis, to Miss Delta Newton of Clifford, September 16.

Clifton Ross Titus to Miss Mildred Carolyn Mitchell, both of Bassetts, Va., October 7.

Frederick S. Wolf, Baltimore, to Miss Betty Saunders Stern of New York, October 4.

Francis J. Robben, Willow Grove, Ohio, to Miss Elizabeth McGary of St. Louis, recently.

Royal V. Sherman, Minneapolis, to Miss Elizabeth Alberts of St. Paul, November 18.

James J. Morrow, Austin, Minn., to Miss Ruth A. Sargent of Red Wing, recently.

Joseph Webb, Springfield, Ohio, to Miss Florence Barlow of Urbana, recently.

Jacob D. Pinson to Miss Leah Freeman, both of Philadelphia, August 3.

Hugh Wellmeier to Miss Helen H. Frazier, both of Piqua, Ohio, October 11.

Burt Hubbard to Miss Stella Carr, both of Lima, Ohio, recently.

Milton Plotz to Miss Helen Ratnoff, both of Brooklyn, recently.

Deaths

Leon Dennis Pierce Clark ● New York; University of the City of New York Medical Department, 1892; member of the Connecticut State Medical Society, the American Neurological Association, American Psychoanalytic Association, American Psychiatric Association and the Association for Research in Nervous and Mental Diseases; member and past president of the National Association for the Study of Epilepsy, American Psychopathological Association, New York Neurological Society and the New York Psychiatric Society; for many years on the staffs of the Manhattan State Hospital, Craig Colony for Epileptics and the New York City Children's Hospital; trustee to the Letchworth Village for Mental Defectives, Thiells, N. Y.; author of "Clinical Studies in Epilepsy," "Psychohistorical Studies of Notable Historic Characters" and of numerous monographs on nervous and mental diseases, and co-author of "Diagnosis of Organic Nervous Diseases" and "Neurological and Mental Diagnosis"; editor of *Archives of Psychoanalysis*, 1926-1927; aged 63; died, December 4, of heart disease.

Frederick Adam Cleland, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1901; assistant professor of obstetrics and gynecology at his alma mater; member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons; fellow of the American College of Surgeons; served as senior surgeon with the Canadian Expeditionary Force in Siberia; on the staffs of the Toronto General Hospital, St. John's Hospital, Grace Hospital and the Women's College Hospital; aged 59; died suddenly, November 26, of heart disease.

William Le Moyne Wills, San Marino, Calif.; University of Pennsylvania School of Medicine, Philadelphia, 1882; member of the California Medical Association; fellow of the American College of Surgeons; formerly professor of clinical surgery, University of Southern California College of Medicine, Los Angeles; at one time member and vice president of the state board of health; for many years on the staff of the Children's Hospital, Los Angeles; aged 80; died, December 3.

David Thomas Bowden, Jr., Leonardtown, Md.; Johns Hopkins University School of Medicine, Baltimore, 1918; at one time assistant professor of epidemiology and public health, University of Oklahoma School of Medicine, Oklahoma City; served during the World War; formerly assistant state health officer in Oklahoma, health officer of Phelps County, Missouri, and St. Mary's County, Maryland; aged 41; was found dead, November 2, of heart disease.

Andrew Jackson Giesy, Portland, Ore.; Jefferson Medical College of Philadelphia, 1882; member of the Oregon State Medical Society; emeritus professor of clinical gynecology, University of Oregon Medical School; at one time member of the city board of health; formerly on the staff of the Good Samaritan Hospital; aged 80; died, November 9, of heart disease.

Richard Frothingham, New York; Harvard University Medical School, Boston, 1892; member of the Medical Society of the State of New York and the American Laryngological Association; formerly assistant professor of otolaryngology, Columbia University College of Physicians and Surgeons; aged 67; died, December 5, of heart disease and pneumonia.

Karl Forbes Snyder ● Freeport, Ill.; Northwestern University Medical School, Chicago, 1902; fellow of the American College of Surgeons; on the staffs of the Evangelical Deaconess, St. Francis and Freeport Methodist hospitals; aged 57; died, November 28, of a self-inflicted bullet wound.

Hartland Cyrus Johnson, St. Paul; College of Physicians and Surgeons of Chicago, 1885; an Affiliate Fellow of the American Medical Association; aged 73; on the staff of St. Luke's Hospital, where he died, November 26, of coronary thrombosis and hypertension.

David Autrey, Marietta, Okla.; Memphis (Tenn.) Hospital Medical College, 1900; member of the Oklahoma State Medical Association; past president of the Carter County Medical Society; formerly county health officer; aged 66; died, November 21, of heart disease.

Francis Regis Harrison, East Liverpool, Ohio; University of Pennsylvania School of Medicine, Philadelphia, 1900; member of the Ohio State Medical Association; on the staff of the East Liverpool City Hospital; aged 54; died, December 3, of heart disease.

Ola Putman ● Marceline, Mo.; Rush Medical College, Chicago, 1901; formerly secretary of the Linn County Medical Society; aged 55; proprietor of the B. B. Putman Memorial Hospital, where he died, December 4, of coronary thrombosis.

Lamartine O. Dudgeon, Sweetwater, Texas; University of Texas School of Medicine, Galveston, 1903; member of the State Medical Association of Texas; on the staff of the Sweetwater Clinic Hospital; aged 57; died, October 1.

Henry Langholz, Oakharbor, Ohio; Northwestern Ohio Medical College, Toledo, 1888; member of the Ohio State Medical Association; aged 74; died, December 8, in the Pool Hospital, Port Clinton, of heart disease.

Alpheus Hartley Wood, Emporia, Va.; Medical College of Virginia, Richmond, 1927; member of the Medical Society of Virginia; aged 35; died, September 28, of acute nephritis and pulmonary tuberculosis.

Charles Elmer Park, Yuankiang, Yunnan, China; Chicago College of Medicine and Surgery, 1913; an Associate Fellow of the American Medical Association; medical missionary; aged 52; died, August 17.

Homer Holcomb Knight, Detroit; University of Minnesota Medical School, Minneapolis, 1930; aged 28; on the staff of the Herman Kiefer Hospital, where he died, October 30, of pneumonia.

Sigismund Emil Prodman, San Francisco; Imperial University of Jurjev, Russia, 1894; Imperial Military Medical Academy, St. Petersburg, Russia, 1902; aged 62; died, August 9.

Thomas Hamilton Burch, Ridgewood, N. J.; University of the City of New York Medical Department, 1880; aged 76; died, November 27, of cerebral hemorrhage and hemiplegia.

James Madison Bannister, Snyder, Texas; Southwestern University Medical College, Dallas, 1907; served during the World War; aged 54; died, October 12, of heart disease.

William B. Johnston, Ellicottville, N. Y.; University of Buffalo School of Medicine, 1881; member of the Medical Society of the State of New York; died, October 23.

Marquis Ernest Gilmore ● Fort Worth, Texas; Northwestern University Medical School, Chicago, 1900; aged 63; was killed, December 2, in an automobile accident.

M. Josephine McChesney, Osceola, Neb.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1888; aged 82; died, November 10, of senility.

Frederick H. Snow, San Diego, Calif.; University of Wooster Medical Department, Cleveland, 1879; aged 79; died, in November, of cerebral hemorrhage.

Clement Tarwell Branch, Camden, N. J.; Howard University College of Medicine, Washington, D. C., 1900; aged 64; died, November 30, of heart disease.

Robert Babcock, Albany, N. Y.; Albany Medical College, 1884; aged 76; died, December 8, of injuries received when he was struck by an automobile.

Lorenzo T. Potter, Jersey City, N. J.; Chicago Medical College, 1880; aged 74; died, November 22, in New York, of carcinoma of the mouth.

Isaac Noel Stowe, Atlanta, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1893; aged 62; died, September 7, of heart disease.

William Harry Tatman, Bellaire, Texas; Medico-Chirurgical College of Kansas City, 1901; aged 64; died, September 19.

Theodore W. Culp, Ava, Ill.; Missouri Medical College, St. Louis, 1888; aged 68; died, November 19, of myocarditis.

William Jackson Cole, South Miami, Fla.; Medical College of Evansville, Ind., 1877; aged 83; died, November 10.

Andrew Adalbert Fabian, Larksville, Pa.; Jefferson Medical College of Philadelphia, 1915; aged 45; died, November 2.

Charles H. Hubbard, Swarthmore, Pa.; Hahnemann Medical College of Philadelphia, 1883; aged 83; died, November 12.

Archibald E. Beaton, Boston; Baltimore Medical College, 1896; aged 66; died, November 23, of coronary thrombosis.

Norman C. Hunter, Laurinburg, N. C.; Medico-Chirurgical College of Philadelphia, 1899; aged 58; died, November 16.

Andrew Patrick Owens, Texarkana, Ark.; Louisville (Ky.) Medical College, 1877; aged 85; died, October 15.

Howard Gray Martin, Los Angeles; Cooper Medical College, San Francisco, 1902; aged 56; died, October 20.

Aubrey Horatio Staples, Oakland, Calif.; Baltimore Medical College, 1896; aged 59; died, October 14.

William Harrison, Marshall, Mo.; St. Louis Medical College, 1874; aged 83; died, September 18.

Bureau of Investigation

AGAIN THE QUESTIONNAIRE NUISANCE

Franklin M. Goodchild, M.D., Turns His Attention from Soaps and Cooking Fats to Motor Cars

Time and again this department of THE JOURNAL has called attention to the plague of questionnaires with which the medical profession is afflicted. Let it be admitted that some responsibility for this condition rests on our profession, because so many of us, with easy-going tolerance, fill out such questionnaires instead of putting them in the ash-can where they belong. Most of these inquiries come from advertising agencies or their satellites. Their object is to get, at the expense of a postage stamp, an "expert opinion" that can be twisted in some way to sustain the "health angle" that the advertising agency wants to use in crying the wares of its clients. Occasionally the questionnaires come frankly from the advertising agencies themselves. These, at least, have the virtue of being above-board, even though the impertinence is not diminished. Many of them, however, are sent out under some high-flown name such as "Modern Research Society," "Medical Research Bureau," "National Research Bureau," or some similar appellation. Occasionally they come out under the name of an individual physician.

The latest questionnaire that has been sent to physicians in the past week comes from Dr. Franklin M. Goodchild, whose stationery carries the address Room 1516, 1250 Sixth Avenue, New York City. Dr. Goodchild, according to the records of the American Medical Association, was born in Philadelphia in 1891, holds a diploma from Columbia University College of Physicians and Surgeons, 1918, and a New York license of the same date. He is not a member of his local medical society or, of course, of the American Medical Association.

The files of the Bureau of Investigation disclose that more than three years ago—in March, 1930—Dr. Goodchild was sending out a questionnaire on the stationery of one Percival White, which described Mr. White as a "Research Counsellor" and Dr. Goodchild as belonging to Mr. White's "Medical Department." Incidentally, the Bureau of Investigation developed the fact that Percival White was one of the owners of an advertising agency known as White and Parton, Inc.

Percival White, through Dr. F. M. Goodchild, was, it seems, interested in having physicians answer five questions relative to the alleged advantages "of the two distinct classes of soap —white soap and colored soap." This calls to mind a similar questionnaire sent out in January, 1929, by the editors of the *Medical Review of Reviews*, who wanted to know of physicians whether they recommended white or colored soap, and those that are perfumed or those that are free from odor. This particular questionnaire was referred to in an article on the subject appearing in this department of THE JOURNAL, March 23, 1929.

Dr. Goodchild in his letter of March 4, 1930, stated that it was his intention to make public "through the daily press and other mediums" the results of his survey of white and colored soap. Sure enough, it was only a few weeks later that there emanated a mimeographed statement sent broadcast to publishers and headed "Physicians Draw Color Line in Soap—White Soap Triumphs Over Colored in National Survey." Then followed a two-and-a-half page article written in the most approved "inquiring reporter" style and said to be "Authorized by F. M. Goodchild, M.D., 25 West 45th Street, New York City" (this was the address of Mr. Percival White of White and Parton, Inc.). Dr. Goodchild's "story" was to the effect that he had received replies on the subject of white and colored soap from 205 physicians and nurses although just what proportion of the 205 were physicians and what proportion were nurses was not stated. Of this group, described as "medical authorities," 199 reported "that they had noticed foreign matter in colored soap, while they had found white soap generally free from it," while only six of the same group "reported that they found no harmful ingredients in colored soap."

Dr. Goodchild's article stated further that "most of the health officers and physicians who expressed themselves believed that colored soap predominated in producing harmful effects," such effects including dehydration dermatitis or other skin trouble, roughness, dryness or chapping. "The white soap, on the contrary, was not observed to disturb the skin." In order, doubtless, to lend an air of verisimilitude to an otherwise bald and unconvincing statement, Dr. Goodchild gave the names and addresses of forty-nine persons who, he claimed, had favored white soap; among these were several physicians who hailed from various parts of the United States. From the east there were six physicians listed, coming from the states of New York, Maryland (two), Vermont, Rhode Island and Ohio. In the middle west nine physicians succumbed to the questionnaire—three from Illinois, two from Michigan, three from Missouri, and one from Indiana. Only two states in the west furnished men who answered Dr. Goodchild's letter: California and Colorado. These, with one physician from West Virginia, completed the list. The remaining names out of the forty-nine given were those of laymen, some of them alleged to be registered nurses, others superintendents of hospitals, sanatoriums and infirmaries. Summed up, according to Dr. Goodchild's "release," one hundred and sixty-three "medical authorities" were said to have "registered themselves in favor of white soap, and only seven for colored." Which must have been very satisfactory for Dr. Goodchild or Mr. White.

As already stated, Dr. Goodchild's interest in the question of the color of soap seemed to extend from March, 1930, until May, 1930. By October, 1930, this inquiring medical reporter had turned his attention to cooking fats, with the very obvious effort to accumulate data to prove that vegetable fats are superior to animal fats for cooking purposes. This time Dr. Goodchild's questionnaire was sent on stationery bearing his name and not that of Mr. White. However, the address was 25 West 45th Street, the address of Percival White and White and Parton, Inc. Was it a case of "the voice is Jacob's voice, but the hands are the hands of Esau?" Dr. Goodchild's vegetable-fat questionnaire went, in addition to physicians, also to those connected with educational institutions, such as those in charge of home economics departments of universities and colleges. The leading character of the doctor's questions can best be brought out by quoting verbatim one or two of them:

"Do you agree that vegetable fats are more wholesome than animal fats because they are cleaner and sweeter and do not so readily undergo decomposition changes?"

"Do you agree or disagree with that medical opinion frequently expressed, that vegetable fats are more digestible than animal fats?"

"In your opinion, are there certain diseases in which a vegetable diet is very important? If so, is gastric ulcer one of them, and what others could you mention?"

Just what results Dr. Goodchild got in his vegetable-fat questionnaire, we do not know, as we were not favored with any mimeographed or other material sent out either by Dr. Goodchild or his employers—if any—on the subject.

Two years later, in October, 1932, Dr. Goodchild had returned to his first love, soap, and was again circularizing physicians, particularly dermatologists. The doctor was still using stationery bearing his name, but his address had changed from 25 West 45th Street to 130 West 42d Street. From the letter sent to physicians, it appears that Dr. Goodchild was greatly concerned over the fact that "the claims of certain soaps for medicinal and antiseptic qualities are greatly exaggerated." He gave it as his opinion, and it is an opinion that all rational people will agree with, that the main function of soap is to cleanse. This was the doctor's thesis, and "in the interests of enlightening the public on the real facts," he was writing to the various physicians and "other leaders" in the field, not, it seems, in order to get an unbiased expression of opinion, but, as he admitted in the introduction to his questionnaire, "to obtain authoritative *confirmation*" of the thesis already laid down. Here again the doctor's questions were strictly leading in character, thus:

"Do you agree that all soaps have antiseptic action, regardless of the addition of any special ingredients?"

"Do you agree that the main function of soap is to cleanse, not to cure?"

"Do you agree that to be suitable for general daily use, a soap should be pure, mild and neutral?"

Just how many replies Dr. Goodchild got and whether they fitted in with the problem that he had, we have no means of knowing. We do know that one well-known dermatologist in the east notified Goodchild very properly that when he gave expert opinion to reputable commercial concerns, he always charged an adequate fee for such work.

In his present questionnaire, Dr. Goodchild abandons what might be called the chemical field—soap and vegetable fats—and enters the mechanical field—motor cars. He is still writing on stationery that carries his name, but the present address given is Room 1516, 1250 Sixth Avenue, New York City. He writes to the physician and asks him, "as a leader in your field," for his views on the "individual springing of automobile wheels or 'knee-action,' as it is sometimes called." Dr. Goodchild then goes on to state the various alleged good points on this "improvement in motor car construction recently pioneered in by General Motors." After detailing the virtues of the improvement—presumably with the idea that the recipient of his letter may realize that Dr. Goodchild wants a favorable report—the doctor states that he is "personally much interested in this development" and asks the doctor to whom he writes whether he does not "agree that this development is worthy of approval." He closes his letter with the statement that unless the physician to whom he writes advises to the contrary, he plans to use the physician's name and statements for publication, "along with those of other leaders."

After this article was in type and ready to go on the press, the Bureau of Investigation learned that Dr. Franklin M. Goodchild is conducting his "survey" in connection with the so-called knee-action in motor car construction for Mr. Percival White, "marketing counsellor," 1250 Sixth Avenue, New York City.

Correspondence

PRODUCTION OF ENDOMETRIAL GROWTH IN CASTRATED WOMEN

To the Editor:—In the discussion of our second experiment, described under the title "Production of Endometrial Growth in Castrated Women: The Minimum Dosage of Theelin That Is Required" (THE JOURNAL, November 4, p. 1466), Dr. Emil Novak states that "the method has been used, as Dr. Werner and Dr. Collier know, particularly by Clauberg and Kaufmann in Germany."

The statement by Dr. Novak is ambiguous. While we were the first to produce the growth phase and uterine bleeding, among other phenomena, in the uterus of castrated women by the use of theelin, one might infer from his discussion that this is not the fact. We believe that Dr. Novak did not intentionally wish to leave this impression. We feel that he wished to convey the fact that Dr. Kaufmann has also done work of this nature and has produced the premenstrual endometrium, but not until after we had completed and published an account of our work with theelin in a preliminary report in the *Proceedings of the Society for Experimental Biology and Medicine* in June, 1932.

As proof of the foregoing statement regarding the priority of our work, we cite the article of Dr. Kaufmann published in the *Zentralblatt für Gynäkolgie* in October, 1932, in which he reports four experiments performed by him:

EXPERIMENT 1.—In 1928 he injected 2,320 mouse units of "follikulin" into a castrated woman over a period of twenty-two days. He states as a result of this treatment that he "was unable to demonstrate any effect on the endometrium of this patient."

EXPERIMENT 2.—In 1930 he injected 21,500 mouse units of "Brunsthormon" over a period of thirty-two days and 42 units of corpus luteum hormone. He states that "curettage following this experiment failed to show any endometrial effect."

EXPERIMENT 3.—In February, 1932, he injected 100,000 units of progynon benzoate in a period of ten days. He states that again he "was unable to produce a functioning endometrium."

EXPERIMENT 4.—In June, 1932, he injected 10,000 units of progynon benzoate daily for twenty-one days (total, 210,000); this was followed by seven daily injections of 5 rabbit units of corpus luteum hormone. He was successful in producing a premenstrual endometrium for the first time by this experiment.

As regards work by Carl Clauberg, an article was published by him in the *Zentralblatt für Gynäkologie*, Oct. 8, 1932, entitled "The Action of the Luteal Hormone, the Specific Hormone of the Corpus Luteum, on the Human Uterus." In this article he remonstrates with Dr. Kaufmann for having claimed priority, but he admits not having published his work up to that time.

In contrast to this work by Kaufmann, we began our first experiment, Jan. 10, 1932, using five castrated women, four of them with intact uteri, while Kaufmann used one castrated woman. During the first twenty-eight day period each patient received 200 Allen-Doisy rat units of theelin daily. Curettements were done before beginning treatment and each week thereafter for three weeks. At the end of two weeks we were able to show marked endometrial growth in all four patients and uterine bleeding during and at the end of the experiment.

This experiment was completed, April 22, 1932, and reported at the St. Louis University seminar in May, 1932; a preliminary report was published in the *Proceedings of the Society for Experimental Biology and Medicine* in June, 1932, at which time Kaufmann was beginning his first successful experiment on one castrated woman, the report of which was not published until October, 1932. Our complete report was accepted for publication in THE JOURNAL in September, 1932, and published in THE JOURNAL, March 4, 1933.

AUGUST A. WERNER, M.D.,
W. D. COLLIER, M.D.,
404 Humboldt Building. St. Louis.

USE OF ERGOT TO CONTRACT CAPILLARIES IN PURPURA

To the Editor:—Recently we have had a patient at Grady Hospital suffering from thrombocytopenic purpura haemorrhagica, probably resulting from intravenous arsenic. He was bleeding continuously from the mucous membranes. There were many large purpuric spots over the body surfaces. The blood examination revealed 2,000,000 red blood cells, 5,000 white blood cells, 65,000 platelets, and clot retraction sixty minutes plus.

Repeated transfusions gave temporary support, yet it seemed that he would bleed to death in spite of all medication.

Finally we administered to him ergot in 1 drachm doses every four hours, and solution of pituitary, 0.5 cc., hypodermically. Following the first two doses of ergot and one hypodermic of pituitary the bleeding diminished. After twenty-four hours slight bleeding again occurred. The medication was repeated, another transfusion was given, and after this his recovery was rapid and progressive. He is now well.

The ergot and solution of pituitary were suggested by me because I have long felt that the pathologic physiology must be intimately related to the capillary bed as well as to the platelet deficiency. It is a well known fact that cessation of hemorrhage depends on the contraction of the vessel wall in connection with other factors. It seemed reasonable that, if the capillary walls could be contracted, the bleeding might be stopped, and to do this the ergot and the solution of pituitary were used. In this one instance the result was gratifying. It may be that there is some equal ratio between capillary distention and platelet efficiency; that is, a widened capillary plus deficient platelets would inhibit the hemorrhage defense, whereas a contracted capillary would be enabled to function even with diminished platelets.

This letter is written so that you may describe this method of treatment for the benefit of other physicians who have such cases. I am anxious to know whether others obtain similar results from this procedure.

Heretofore, these patients have been treated with transfusions and other supportive measures. A few spleens have been removed. The mortality has been most discouraging.

The pharmacologists seem to be in dispute as to whether ergot contracts the capillaries or not; it is agreed, however, that the smaller vessels with muscular walls are affected. This may in time aid in contracting the smaller terminals. Solution of pituitary is believed to contract the smaller arterioles and capillaries.

JACK C. NORRIS, M.D., Atlanta, Ga.
Pathologist, Grady Hospital.

HISTORICAL ASPECTS OF ENZYME INVESTIGATIONS

To the Editor:—THE JOURNAL has presented an editorial discussion of the historical aspects of enzyme investigations (The Centenary of the Discovery of Diastase, November 11, p. 1564), which I have read with great interest. Certainly all workers in this field are pleased to see the emphasis placed on the application of this study to the basic medical sciences.

Priority as regards the first scientific description of enzyme activity is apparently not a matter of general agreement and I should like to call attention to some early observations that are quite commonly overlooked. Practically all books on the subject, for instance, place the priority with Dubrunfaut and with Payen and Persoz in 1830 and 1833, respectively, and this has naturally been accepted in the editorial mentioned. The first description of a practical preparation of an active "diastase" product was, no doubt, that by Payen and Persoz. However, in referring to the first observation of enzyme activity, usually no reference is made to the report by G. S. C. **Kirchhoff**, read before the Royal Academy of St. Petersburg in **1814**, "Ueber die Zuckerbildung beim Malzen des Getreides, und beim Bebruehen seines Mehls mit kochendem Wasser" (*J. f. Chemie u. Physik*, Schweigger's, Nuremberg **14**:389-398, 1815). An English abstract of this report was as follows:

> A glutinous constituent is separated from wheat meal by washing and is mixed with a paste of potato starch. The pasty stiffness soon disappears and a sugar is formed. The yield of sugar is markedly affected by the experimental temperature, a temperature of 50 to 75 appearing most favorable. The syrup has the sweetness of malt syrup, is fermentable and is partially soluble in alcohol. The soluble component crystallizes from alcohol in very small, white crystals. The insoluble component dissolves in water, is not precipitated by an infusion of nutgalls, and appears to be a modified form of starch. The active glutinous material is almost entirely recovered by filtration; the filtrate is capable of partially converting a fresh quantity of starch. Dilute sulphuric acid completely prevents conversion of starch by the gluten; KOH also deprives the gluten of its activity. Concludes that the formation of sugar in malt is explained and that a starch-sugar transformation is a necessary step in the alcoholic fermentation of amylaceous materials.

This article can be interpreted to include the aspect of separating a crude enzymic agent, a recognition of its catalytic nature and a rough description of its optimum conditions of activity. Although I have emphasized this priority in two books, "A Comprehensive Survey of Starch Chemistry" and "Enzyme Actions and Properties," it has not been recognized by some subsequent books on the subject. This is probably not based on any discrimination or conflicting interpretation but merely on the relative inaccessibility of the reference in question. Apparently the only available set of this journal is in the New York Public Library, at least in America.

Having spent a good deal of time on this point, I was interested to note that priority was really given to Kirchhoff in most discussions up until about 1850 or 1875, and after that

the more ready accessibility of the references to Dubrunfaut and Payen and Persoz simply displaced the priority due Kirchhoff.

Again may I emphasize my agreement with the spirit and general context of the editorial mentioned.

ROBERT P. WALTON,
Tulane University School of Medicine,
New Orleans.

Queries and Minor Notes

ANONYMOUS COMMUNICATIONS and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted, on request.

SENSITIZATION TO NEOARSPHENAMINE

To the Editor:—A woman, aged 35, acquired syphilis and came to me with a secondary rash, condylomas, and a 4+ Wassermann reaction. I gave her 0.3 Gm. of neoarsphenamine the first time and 0.45 Gm. the next. The night of the second injection she had chills and fever, which recurred daily until a morbilliform rash appeared five days later. I then put her on 0.5 Gm. of sodium thiosulphate every two days, and the rash is almost gone. I am asking you for a complete outline for her further treatment. Shall I turn to bismuth, and how much shall I give? May I ever use neoarsphenamine again and, if so, in what dosages? Is mercury indicated and, if so, in what form and dosages? Please answer this as soon as possible, as I would like to continue this treatment without delay. Kindly omit name.

M.D., Pennsylvania.

ANSWER.—It is impossible to be sure at present whether this patient has been permanently sensitized against neoarsphenamine. Morbilliform rashes may or may not be the precursors of an exfoliative dermatitis and an expression of permanent sensitization. In view of the fact that the patient has a recent syphilitic infection, it is of the utmost importance to determine this point as promptly as possible; if she is not permanently sensitized, the total duration of her treatment may be much shorter and the hope of an ultimately successful outcome much better than if treatment must be carried on with the heavy metals alone.

There should be no interruption in the continuity of treatment because of this reaction; intramuscular injections of bismuth salicylate, 0.2 Gm. suspended in oil, should be started at once and continued weekly for six weeks. Toward the end of this course of bismuth therapy the sensitivity of the patient for the arsphenamine (including arsphenamine and silver arsphenamine as well as neoarsphenamine) should be tested by means of a patch test (technic described by Schoch, THE JOURNAL, April 16, 1932, p. 1367). If this test is positive (erythema and vesiculation appearing in the tested area in from twenty-four to forty-eight hours), no further arsphenamine may be administered at any time; the patient is permanently sensitized. While a positive patch test indicates sensitization, however, a negative test does not exclude it. Further work with the test has shown that not infrequently it may be negative in an individual who is definitely known to be sensitive.

If the patch test is negative, sensitivity should be tested by cautious intravenous testing. For this purpose, a different arsphenamine product from that originally used should be chosen since, in a few instances, sensitization may be actually drug specific rather than group specific. In this instance, silver arsphenamine is the drug of choice for this purpose. The initial dose should be minute: 25 mg. (0.025 Gm.). The patient should be carefully observed and interrogated for the possible appearance of four phenomena: generalized itching in the absence of a skin rash, the appearance of any skin eruption, fever, and malaise—a knocked-out feeling out of proportion to the size of the dose administered. If any of these phenomena are present, sensitization may be assumed, and the arsphenamines must be permanently discontinued. If none of them are present, the dose may be cautiously increased each week by equally small increments (0.025 Gm.), until either evidences of toxicity appear or an average therapeutic dose is reached. Thus, it will take about ten weeks of careful dosage increase—0.025, 0.05, 0.075, 0.1 Gm., and so on—to attain the therapeutic dose of silver arsphenamine of from 0.2 to 0.3 Gm. The appearance of toxic phenomena (itching, dermatitis, fever, prolonged malaise) at any time is a signal for the end of all attempts at arsphenamine therapy.

During this course of intravenous testing, it is desirable also to perform frequently repeated leukocyte and differential counts. Leukopenia, especially if accompanied by a decrease in granulocytes, is a warning of impending serious trouble; so also is eosinophilia, even if the total white count remains normal.

If either the patch test or the cautious intravenous test already described shows that the patient is sensitized, further treatment must consist of the heavy metals alone. These also should be given continuously if possible, the best method being courses of intramuscular injections of an insoluble bismuth salt, preferably the salicylate, alternating with courses of mercury by inunction. Under these circumstances, the total duration of treatment must be a minimum of three years instead of the average of from fifteen to eighteen months if an arsphenamine can be used.

The spinal fluid should be tested as a routine in any case at the end of about six months of treatment. Should it prove to be positive, it is worth while noting that arsphenamine sensitive patients may be given tryparsamide, a pentavalent drug especially valuable in neurosyphilis, without danger of producing dermatitis.

Incidentally, some workers feel that sodium thiosulphate is of no value whatever in poisoning with the arsphenamines or with other metals. Calcium is probably much more effective.

TENDON TRANSPLANTATION AFTER CUTTING POSTERIOR INTEROSSEOUS NERVE

To the Editor:—Assuming that the posterior interosseous nerve is cut at a point about two inches below the radial head or at the radial head, is there any tendon transplantation operation or any operation that will restore extension at the metacarpophalangeal joints and phalanges? Please omit name.

M.D., New York.

ANSWER.—The subject of peripheral nerve injuries and their treatment received a great stimulus during the World War from the efforts of Sir Robert Jones, Sir Harold Stiles, C. L. Starr, Arthur Steindler, Harry Platt, Dean Lewis, Delagenière, Walther, Tinel and Binesty.

Failures or partial failures after operations on the musculospiral nerve have been successfully treated by tendon transplantation. The operation of Sir Robert Jones of Liverpool consists in the transplantation of the (1) pronator radii teres into the extensores carpi radiales longior and brevior; (2) flexor carpi ulnaris into the extensor communis digitorum and extensor longus pollicis; (3) flexor carpi radialis into the extensor ossis metacarpi pollicis and extensor brevis pollicis.

The results of this operation are striking, a useful and strong hand being obtained—a hand that can be utilized for most of the ordinary occupations. On page 18 of his little book called "Notes on Military Orthopaedics," published by Cassell & Co., Ltd., London, Sir Robert Jones states that in cases of musculospiral injury the uncontrolled action of the flexor group causes the fingers to curl into the palm and the hand to become useless. In such a case (*a*) the flexor carpi radialis and the flexor carpi ulnaris can be transplanted into the paralyzed extensor of thumb and fingers and, (*b*) in addition, the pronator radii teres may be sutured to the two radial extensors.

Jones recommended transplantation of the pronator radii teres and the radial and ulnar flexors in musculospiral paralysis and describes the technic as follows: With the forearm midway between pronation and supination, an incision is made along the radial border of the forearm in its middle third. Under cover of the tendon of the supinator longus, the pronator radii teres will be found where it becomes inserted into the outer border of the radius. From this it is detached and is then inserted into the tendons of the extensor carpi radialis longus and brevis, which lie closely applied to it on the dorsal surface.

A horseshoe incision, with the convexity resting on the back of the carpus, with the two straight sides extending along the radial and ulnar borders, is now made. Through the lateral aspects of this incision the tendons of the carpi ulnaris and radialis are identified and are detached from their insertions as near the carpus as possible.

The tendons are brought round the ulna and radius respectively in a very slanting fashion and are then attached to the extensors of the fingers and thumb, the flexor carpi ulnaris being attached to the extensor longus digitorum tendons of the three inner fingers and the flexor carpi radialis to those of the thumb and index finger.

When the lesion is below the origin of the posterior interosseus nerve, the radial extensors of the wrist are intact and the transference of the pronator radii teres is, of course, unnecessary. Stiles modified the original operation by inserting the tendon of the palmaris longus into the extensor pollicis longus; the flexor carpi radialis into the extensor primi internodii pollicis and the extensor ossis metacarpi pollicis; and the flexor carpi ulnaris into each of the extensor digitorum tendons. The hand is immobilized for two weeks in dorsiflexion, the wrist being kept almost at a right angle, and the metacarpophalangeal and interphalangeal joints being only slightly palmar flexed

to avoid subsequent stiffness. The after-treatment consists of daily massage and electrical stimulation. Recovery is usually complete in from eight to ten weeks, and the position of extension must be maintained until there is return of voluntary function.

The following books and articles may be consulted for further details:

Campbell, W. C.: A Text Book on Orthopedic Surgery, Philadelphia, W. B. Saunders Company, 1930.

Jones, Robert: Tendon Transplantation in Cases of Musculospiral Injuries Not Amenable to Suture, *Am. J. Surg.* **35**:333 (Nov.) 1921.

Stiles, H. J.: Operative Treatment of Nerve Injuries, *Am. J. Orthop. Surg.* **16**:351 (June) 1918.

Steindler, Arthur: Operative Orthopedics, New York, D. Appleton & Co., 1925, p. 89.

McMurray, T. P.: *J. Orthop. Surg.* **1**:125 (March) 1919.

PERTUSSIS VACCINE

To the Editor:—What is the value of pertussis vaccine as a preventive measure and as a measure for reducing the severity of the attacks? When vaccines can be counted on as reliable? Please omit name.

M.D., Rhode Island.

ANSWER.—There is considerable difference of opinion among physicians with regard to the value of pertussis vaccine either as a preventive or as a therapeutic measure. Many believe that pertussis vaccine prepared entirely from the Bordet bacillus is a distinct aid as a prophylactic. Some of the vaccines used for the treatment of whooping cough are termed "pertussis combined" and contain, in addition to the Bordet bacillus, staphylococci, streptococci, pneumococci, influenza bacilli and Micrococcus catarrhalis. Though many physicians favor the use of vaccine in the treatment of whooping cough, there seems to be little doubt based on numerous reports and investigations that have been carried on in the past that the average stock vaccine supplied for the treatment of this disease exerts little, if any, influence on the course during the paroxysmal stage.

PHYSIOLOGIC BASIS FOR HYPERACTIVE CHILD

To the Editor:—Can you give me any information regarding the physiologic basis for the overactive or hyperactive child? Please omit name.

M.D., Rhode Island.

ANSWER.—A physiologic basis for the overactive or hyperactive child may be sought in the autonomic nervous system, the endocrine glands or the constitutional makeup of the individual. Existing knowledge of the physiologic regulation of the vegetative nervous system is in a highly speculative state. However, in many of these overactive children an accompanying increased salivary gland secretion, increased intestinal motility and vasomotor instability can lead one to suspect a hyperactivity in the autonomic system. The relation of the endocrine glands to overactivity in children is founded on better known physiologic facts. The influence of the thyroid secretion, as, for example, the hyposecretion in cretinism, with accompanying dulness and sluggishness, and the overactivity of the hyperthyroid, are examples of knowledge in this field. The endocrine influence in the growing child, especially at the time of puberty, is well known. A physiologic increase in systolic blood pressure at this period, often to astonishingly high values, is based on physiologic endocrine influence. The constitutional factor is most important. Overactive children are most often the offspring of highly strung, emotional, unstable parents. A child who inherits an unstable nervous system or a temperamental emotional disposition can hardly be expected to be dull, inactive and phlegmatic in his reaction. Environment also may tend to produce or aggravate overactivity. Calm, placid surroundings constitute the ideal environment for every child. A child with an overactive tendency will show more pronounced and aggravated symptoms in the overactive direction in a disturbed and turbulent home life.

THERAPEUTICS OF CALCIUM

To the Editor:—What are the more common indications for calcium therapy at the present time? Please omit name.

M.D., Rhode Island.

ANSWER.—Calcium carbonate is employed as a vehicle for antacid action.

Calcium is employed as a vehicle for ions with a systemic acidifying tendency; e. g., calcium chloride as a diuretic.

Calcium is used to prevent calcium impoverishment of the system, for example, in pregnancy and lactation and in childhood, unless the calcium is taken in the form of milk (1 quart daily).

In the treatment of acid diarrhea, calcium carbonate not only neutralizes the acids and thus checks the irritation but also raises the amount of calcium available for absorption, which may be of importance in celiac disease of infants and sprue in adults.

In tetany and spasmophilia there is a deficiency in available calcium ions, owing to alkalosis or parathyroid deficiency. Hence calcium administration is of but temporary value in these conditions, unless the alkalosis or parathyroid deficiency is simultaneously corrected.

The results from calcium salts in inflammatory and noninflammatory effusions and edemas is generally disappointing, unless the ionization of calcium is at the same time increased, as it may be by the intravenous injection of calcium chloride. Simultaneous salt restriction seems to be especially important for results in tuberculous effusions.

While calcium cannot, in general, be relied on to increase the coagulability of the blood, it may do so in certain conditions, as in the bleeding tendency of the icteric.

The local use of calcium in the form of lime water or of chalk exerts a very mild astringent effect.

STRICTURE OF THE CERVIX WITH HEMATOMETRA

To the Editor:—A single woman, aged 24, with a normal genital history up to three years ago, when she had gonorrhea, presented herself today with an amenorrhea of two months. She suspected a pregnancy. During her gonorrheal infection she apparently had had some form of thermal cauterization of the endocervix. She was under treatment for about six months and was discharged as cured. Since her gonorrhea, she has menstruated every twenty-eight days up until two months ago, but has had an increasing dysmenorrhea. On examination I found her to be normal in every way except that the external os was completely bridged over by epithelium—not the slightest opening could be found. What, if any, will be the effect on the general health of this individual so long as the occlusion is permitted to remain? Will nature, as a result of the occlusion, abstain from having her ovulate? Please omit name.

M.D., Wisconsin.

ANSWER.—The patient is probably not pregnant but should have an Aschheim-Zondek test to determine this with certainty. The trouble is apparently a stricture of the cervix complicated by hematometra. In the absence of pregnancy, a thorough dilation of the cervical canal is imperative. Otherwise the backpressure of retained menstrual blood will cause hematosalpinx and generalized pelvic inflammation. Ovulation will not cease, but sterility usually occurs in these cases unless the stricture is overcome during the early months.

RELATION OF NASAL OBSTRUCTION TO HEART DEFECT

To the Editor:—A girl, aged 3½ years, has had one attack of rheumatic heart disease, has an autumnal hay fever, and has frequent colds. Her tonsils and adenoids do not appear to be enlarged. However, the septum of her nose deviates markedly to the left at the level of the upper edge of the lowest turbinate bone. The obstruction is so great that even when well she has difficulty in breathing through her nose. She wakens at night frequently because of inability to get her breath, but she never breathes through her mouth. The hay fever aggravates the condition greatly. Will not the difficulty in breathing in time damage her already slightly weakened heart? Under the circumstances, is operation to straighten the septum advisable? What sort of operation should be done? Please omit name.

M.D., Michigan.

ANSWER.—The marked difficulty in breathing is not likely to impair a slightly weakened heart, although it may be distressing from the standpoint of both the patient and the parents. The size of the adenoids should be estimated by finger palpation and judgment drawn not only from the actual size of the adenoid mass but from a comparison between its size and that of the nasopharynx. A small adenoid will markedly block a small nasopharynx, and its removal, by the same token, will much improve the breathing. As to the additional troubles imposed by the deviated septum, a child whose difficulties are as great as those described might, in the opinion of many good men, be submitted to a septum operation. Such occasions are not frequent, of course, but from time to time they do occur. As the deviation in these instances is frequently anterior and cartilaginous in nature, the removal of just the offending piece of cartilage may solve the whole problem, no more tissue being taken out than is absolutely necessary. A skilful operator may avoid removing any cartilage by incising it in such a fashion that it may be swung into proper position and allowed to remain in place. A cautious procedure would consist in first removing the adenoid mass, proceeding to the septum operation only if this fails to give relief.

The frequent colds must be considered a cause of nasal obstruction, as they may be due to sinusitis with secretion or to a perennial hay fever or vasomotor rhinitis, and these possibilities should be disposed of before surgical intervention is attempted.

RETARDATION OF DEVELOPMENT OF GENITALIA

To the Editor:—Thirteen months ago a boy was born as the second child to two healthy parents. The child has developed normally to the present time. A matter of concern both to the parents and to myself is the small size of the penis, which protrudes hardly noticeably. Circumcision was performed at 1 week of age, revealing the normal glans penis. There seems to be no evidence of hermaphroditism. My prediction is that this will maintain its proportional size, that it is more a congenital deformity than a glandular deficiency. Can you throw any light on this subject? Please omit name.

M.D., Tennessee.

ANSWER.—The condition referred to is often combined with delayed descent of the testicles, which phenomenon should be investigated. Besides individual variations, retardation of development corrects itself frequently with the natural growth of the child. The same holds good in a great many instances with the spontaneous descent of the testicles. Some observers report that in the second year of childhood both these conditions are favorably influenced by the injection of compounds derived from the anterior half of the pituitary body. These compounds may be obtained from any medical supply house.

X-RAYS OR RADIUM IN UTERINE HEMORRHAGE

To the Editor:—In the hands of experts, which has proved the safer measure to use in uterine bleeding of a young woman, x-rays or radium? Please omit name.

M.D., New York.

ANSWER.—A few men employ small doses of radium for bleeding, but the x-rays and radium both cripple the ovaries and on this account most gynecologists do not favor their use in women under 40. Keene gives 100 mg. for not longer than five or six hours, with the thought that the ovaries will not be permanently injured by this small dosage, and produces temporary amenorrhea in this way. Those who are less enthusiastic over fractional doses of radium do not, as a rule, favor the x-rays but prefer recourse to operation in case simple palliative measures are of no avail.

Provided ray therapy has been decided on, radium is usually given preference over the x-rays, first because a diagnostic curettage may be performed at the same time, and this is usually essential, and also because radium is more direct and more localized in its action and the dosage can be accurately gaged.

HIGH BASAL METABOLIC RATE

To the Editor:—Please tell me what a metabolism test of plus 17 for a girl, aged 8, means. Please omit name and address.

M.D., South Carolina.

ANSWER.—A basal metabolism reading of plus 17 for a girl, aged 8 years, must be interpreted with a great deal of caution. Even when such variables as cooperation and emotion have been ruled out, it must be remembered that this result is not much outside the limits of normal variation. It is well to recalculate such a result on the basis of more than one of the prediction standards available for that sex and age. These standards may yield results in a particular case which differ from each other by more than the reading obtained here. This is partly due to the different criteria on which these standards are based, partly because of the fact that there may occur real differences in temporal and physiologic age and partly because, during that decade, small differences in age may have great influence on the metabolic rate. In cases like this, the basal metabolic rate by any one prediction standard may be useful as a guide to the progress of the case or to the effect of treatment. It should not, however, be allowed to outweigh the clinical diagnosis.

TENDER FEET

To the Editor:—A man, aged 71, suffers a great deal from tender feet. While he was in the railway service about thirty-five years ago both of his feet were frozen, but on reaching the hospital his feet were immersed in ice water and he suffered no sloughing or bad after-effects. Since that time his feet have been exposed to extreme cold but never frozen. He does not complain of pain, unless pressure is applied, but of extreme tenderness. Will you please suggest applications that will toughen the skin on his feet? Please omit name.

M.D., Oklahoma.

ANSWER.—The probability is that the trouble is circulatory. Are the feet cold and can a normal pulse be felt in the dorsalis pedis and posterior tibial arteries? Hot foot baths should be followed by the application of an oil. The French advise the use of cod liver oil for this purpose, combined with the administration of small doses of iodides internally. Massage should be done upward with the oil, as the patient can stand it. Tobacco should not be used. Loose fitting shoes and wool socks should be worn. A galvanic foot bath for from ten to fifteen minutes several times a day may be helpful.

Council on Medical Education and Hospitals

COMING EXAMINATIONS

ALABAMA: Montgomery, Jan. 9-13. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written (Group I) (Candidates).* The examinations will be held in various cities of the United States and Canada, April 7. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: Cleveland, June 11. Sec., Dr. William H. Wilder, 122 S. Michigan Blvd., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: Cleveland, June 11. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

ARIZONA: Phoenix, Jan. 2-3. Sec., Dr. J. H. Patterson, 320 Security Bldg., Phoenix.

COLORADO: Denver, Jan. 2. Sec., Dr. Wm. Whitridge Williams, 422 State Office Bldg., Denver.

CONNECTICUT: *Basic Science.* New Haven, Feb. 10. *Prerequisite to license examinations.* Address, State Board of Healing Arts, 1895 Yale Station, New Haven.

DISTRICT OF COLUMBIA: Washington, Jan. 8-9. Sec., Dr. W. C. Fowler, 203 District Bldg., Washington.

HAWAII: Honolulu, Jan. 8-11. Sec., Dr. James A. Morgan, 48 Young Bldg., Honolulu.

ILLINOIS: Chicago, Jan. 23-25. Supt. of Regis., Dept. of Regis. and Edu., Mr. Eugene R. Schwartz, Springfield.

MINNESOTA: *Basic Science.* Minneapolis, Jan. 2-3. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Regular.* Minneapolis, Jan. 16-18. Sec., Dr. E. J. Engberg, 350 St. Peter St., St. Paul.

NATIONAL BOARD OF MEDICAL EXAMINERS: The examinations will be held at centers in the United States where there are five or more candidates, Feb. 14-16, May 7-9, June 25-27, and Sept. 12-14. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

NEBRASKA: *Basic Science.* Lincoln, Jan. 9-10. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEW YORK: Albany, Buffalo, New York and Syracuse, Jan. 29-Feb. 1. Chief, Professional Examinations Bureau, Mr. Herbert J. Hamilton, Room 315 Education Bldg., Albany.

NORTH DAKOTA: Grand Forks, Jan. 2. Sec., Dr. G. M. Williamson, 4½ S. 3rd St., Grand Forks.

OREGON: Jan. 2-4. Sec., Dr. Joseph F. Wood, 509 Selling Bldg., Portland.

PENNSYLVANIA: Philadelphia, Jan. 2-6. Sec., Mr. W. M. Denison, 400 Education Bldg., Harrisburg.

RHODE ISLAND: Providence, Jan. 4-5. Dir., Dr. Lester A. Round, 319 State Office Bldg., Providence.

SOUTH DAKOTA: Pierre, Jan. 16-17. Dir., Dr. Park B. Jenkins, Pierre.

VERMONT: Burlington, Feb. 7-9. Sec., Dr. W. Scott Nay, Underhill.

WASHINGTON: *Basic Science.* Seattle, Jan. 11-12. *Regular.* Seattle, Jan. 15-16. Dir., Mr. Harry C. Huse, Olympia.

WISCONSIN: Madison, Jan. 9-11. Sec., Dr. Robert E. Flynn, 401 Main St., LaCrosse.

WYOMING: Cheyenne, Feb. 5. Sec., Dr. W. H. Hassed, Capitol Bldg., Cheyenne.

Ohio June Examination

Dr. H. M. Platter, secretary, Ohio State Medical Board, reports the oral, written and practical examination held in Columbus, June 6-9, 1933. The examination covered 10 subjects and included 80 questions. An average of 75 per cent was required to pass. Two hundred and forty-two candidates were examined, 238 of whom passed and 4 failed. The following colleges were represented:

College	PASSED	Year Grad.	Per Cent
Northwestern University Medical School		(1933)	83.6, 85.9
Rush Medical College		(1933)	85.3
Indiana University School of Medicine		(1933)	85.2
University of Louisville School of Medicine		(1933)	82.6, 82.7
Harvard University Medical School		(1931)	84.2, 85.9, (1933) 87
Tufts College Medical School		(1932)	81.8
University of Michigan Medical School		(1932)	81.2
University of Rochester School of Medicine		(1932)	85.3, (1933) 80.7
Ohio State University College of Medicine	76.4, 78.4, 79.2, 79.3, 79.4, 79.9, 80, 80.1, 80.2, 80.2, 80.2, 80.4, 80.5, 80.6, 80.6, 80.9, 80.9, 81.1, 81.2, 81.3, 81.3, 81.4, 81.4, 81.5, 81.6, 81.6, 81.8, 82, 82.2, 82.3, 82.3, 82.3, 82.4, 82.4, 82.4, 82.5, 82.6, 82.6, 82.6, 82.6, 82.8, 82.9, 83, 83.1, 83.1, 83.2, 83.2, 83.3, 83.3, 83.3, 83.4, 83.4, 83.5, 83.5, 83.5, 83.6, 83.8, 83.8, 84, 84.4, 84.7, 84.8, 84.8, 85, 85.1, 85.1, 85.7, 85.8, 85.8, 85.9, 86, 86.1, 86.3, 86.4, 86.7, 86.8, 86.8, 87, 87.3, 87.4, 87.5, 88.7, 89.2	(1933)*	78.6, 78.7, 78.8, 79.4, 79.7, 79.7, 79.9, 80, 80.1, 80.7, 80.8, 80.9, 80.9, 81, 81, 81.1, 81.1, 81.2, 81.2, 81.2, 81.3, 81.4, 81.4, 81.6, 81.7, 81.8, 82, 82, 82.1, 82.3, 82.3, 82.3, 82.4, 82.4, 82.4, 82.4, 82.5, 82.7, 82.8, 82.9, 83, 83, 83.2, 83.4, 83.5, 83.6, 83.6, 83.6, 83.8, 83.9, 84.1, 84.2, 84.5, 84.5, 84.6, 84.6, 84.7, 84.8, 84.8, 85, 85.2, 86, 86.3, 86.6, 87.4, 89.1

Western Reserve University School of Medicine (1933) 75.4, 77.9, 79.4, 80, 80.5, 80.7, 80.9, 81.1, 81.2, 81.8, 82.2, 82.4, 82.5, 82.5, 82.6, 82.7, 82.8, 83.2, 83.2, 83.3, 83.3, 83.4, 83.4, 83.7, 83.8, 83.9, 84, 84, 84.1, 84.3, 84.3, 84.4, 84.4, 84.6, 84.7, 84.8, 84.9, 85, 85.3, 85.3, 85.6, 85.7, 85.7, 86.2, 86.2, 86.4, 86.6, 86.8, 86.8, 86.9, 87.1, 87.4, 87.6	(1932)	80.2,
Hahnemann Medical College and Hosp. of Philadelphia (1932) 82.7		82.2,
Jefferson Medical College of Philadelphia (1932) 84.8, (1933) 81.6, 82.6	(1931)	87.8,
University of Pennsylvania School of Medicine	(1931)	80.3
Woman's Medical College of Pennsylvania	(1932)	82.7, 86.3
Marquette University School of Medicine	(1933)	84
University of Toronto Faculty of Medicine (1931) 77.2, (1932) 79.3	(1930)	76.
McGill University Faculty of Medicine	(1933)	77.7
Leopold-Franzens-Universität-Medizinische Fakultät, Austria	(1932)	81.1
Regia Università di Palermo degli studi. Facoltà di Medicina e Chirurgia	(1924)	75
University of Edinburgh Faculty of Medicine	(1931)	75.1

College	FAILED	Year Grad.	Per Cent
Magyar Királyi Erzsébet Tudományegyetem Orvostudományi, Hungary		(1924) 64.9, (1926)†	68.8
Regia Università di Napoli. Facoltà di Medicina e Chirurgia		(1925)	64.6
Universitatea Regele Ferdinand I-iu din Cluj Facultatea de Medicină și Farmacie, Rumania		(1924)†	71.8

Forty-one physicians were licensed by reciprocity and one by endorsement, July 11. The following colleges were represented:

College	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Colorado School of Medicine		(1931, 2)	Colorado
George Washington University School of Medicine		(1929)	Maryland
Emory University School of Medicine		(1929)	Georgia
Rush Medical College		(1931)	Illinois
Indiana University School of Medicine		(1931), (1932)	Indiana
University of Kansas School of Medicine		(1932)	Kansas
University of Louisville School of Medicine		(1931), (1932, 4)	Kentucky
Tulane University of Louisiana School of Medicine		(1931)	Louisiana
Johns Hopkins University School of Medicine		(1928)	Missouri
Harvard University Medical School		(1917)	New York
University of Michigan Medical School (1931), (1932, 2)		(1929),	Michigan
St. Louis University School of Medicine		(1932, 10)	Missouri
Washington University School of Medicine		(1930)	Missouri
University of Rochester School of Medicine		(1931)	W. Virginia
Jefferson Medical College of Philadelphia (1928) Pennsylvania		(1922)	W. Virginia,
Temple University School of Medicine		(1921)	Penna.
University of Pittsburgh School of Medicine		(1931)	Penna.
Vanderbilt University School of Medicine		(1928), (1931)	Tennessee
Medical College of Virginia		(1926)	Virginia
Medizinische Fakultät der Universität Wien		(1901)†	Maryland
Magyar Királyi Ferencz József Tudományegyetem Orvostudományi, Hungary		(1914)†	Indiana

College	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Harvard University Medical School		(1930)	N. B. M. Ex.

* These applicants have received an M.B. degree and will receive an M.D. degree on completion of internship.
† Verification of graduation in process.

Iowa September Examination

Mr. H. W. Grefe, director, Division of Examinations and Licenses, reports the written examination held by the Iowa State Board of Medical Examiners, Sept. 12-14, 1933. The examination covered 8 subjects and included 100 questions. An average of 75 per cent was required to pass. Nine candidates were examined, 8 of whom passed and 1 failed. The following colleges were represented:

College	PASSED	Year Grad.	Per Cent
University of Arkansas School of Medicine		(1933)*	89
College of Medical Evangelists		(1931)	88.1
University of California Medical School		(1921)	89.4
Northwestern University Medical School		(1933)	86
University of Illinois College of Medicine		(1933)†	88.1
Harvard University Medical School		(1928)	88.8
University of Minnesota Medical School		(1933)	87.3
Regia Università di Firenze degli studi. Facoltà di Medicina e Chirurgia		(1925)	85.1

College	FAILED	Year Grad.	Per Cent
Keokuk Medical College, Iowa		(1904)	67

* License withheld pending completion of internship.
† This applicant has completed his medical course and will receive his M.D. degree and Iowa license on completion of internship.

Arizona October Report

Dr. J. H. Patterson, secretary, Arizona State Board of Medical Examiners, reports the written examination held October 3-4, 1933. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Seven candidates were examined, 5 of whom passed and two failed. Seven physicians were licensed by reciprocity and 3 by endorsement. The following colleges were represented:

College	PASSED	Year Grad.	Per Cent
Rush Medical College		(1933)	78.1
University of Kansas School of Medicine		(1931)	81
St. Louis University School of Medicine		(1932)	75, 79.5
McGill University Faculty of Medicine		(1933)	76.7

College	FAILED	Per Cent
Osteopaths		69.8, 71.1

College	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Chicago College of Medicine and Surgery		(1915)	Illinois
University of Louisville Medical Department		(1910)	Kentucky
University of Michigan Medical School		(1929)	Michigan
Washington University School of Medicine		(1930)	Missouri
John A. Creighton Medical College		(1919)	Kansas
Vanderbilt University School of Medicine		(1929)	Tennessee
Dalhousie University Faculty of Medicine		(1932)	Nova Scotia

College	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists		(1933)	N. B. M. Ex.
Albany Medical College		(1929)	N. B. M. Ex.
Medical College of Virginia		(1930)	N. B. M. Ex.

Book Notices

Infections of the Hand: A Guide to the Surgical Treatment of Acute and Chronic Suppurative Processes in the Fingers, Hand and Forearm. By Alfred B. Kanavel, M.D., Sc.D., Professor of Surgery, Northwestern University Medical School, Chicago. Sixth edition. Cloth. Price, $6. Pp. 852, with 216 illustrations. Philadelphia: Lea & Febiger, 1932.

This book has established itself as a classic. It is the work of the best known authority on the subject and presents a complete study of the anatomy, pathology and treatment of infections of the hand. The author has added much new material and radically revised the old. The new material consists of investigations on special infections such as bites and injuries from the teeth, metacarpophalangeal infections, gangrenous infections, and injuries from indelible pencils and cattle hair. Chapters have been added on the function of the hand and the use of splints, and the prophylactic treatment of injuries. Practically every chapter has been brought down to date. In this edition the subject matter is presented with the discussion of the anatomy and the experimental investigation separated from the clinical study. Kanavel emphasizes the fact that lymphangitis and suppurative tenosynovitis are still too often unrecognized and improperly treated. In lymphangitis, hasty incision not infrequently leads to unnecessary loss of life. In suppurative tenosynovitis the pathologic condition is not recognized, and failure to institute early treatment leads to prolonged illness and permanent disability. The chapter on the use of splints after infections of the hand is highly instructive. The chapter on function of the hand in relation to infections is itself worth the price of the book. The composition, including the printing and the paper, is excellent. The illustrations, including line drawings, anatomic dissection, colored diagrams and reproductions of photographs, each and every one of which illustrates at least one point, are instructive. Many of the author's original hand drawings have been replaced by excellent sketches by Tom Jones, who has drawn several illustrations from the author's film on the diagnosis and treatment of infections of the hand. The book should be on the desk of every physician and surgeon. It is indispensable for traumatic surgeons.

Le métabolisme de l'azote: Déperdition, besoins, couverture. Par Emile F. Terroine, professeur à l'Université de Strasbourg. Les problèmes biologiques, XVIII. Boards. Price, 125 francs. Pp. 382, with 21 illustrations. Paris: Les Presses Universitaires de France, 1933.

This volume presents a detailed survey of the whole field of nitrogen metabolism by a competent authority. Through the excellence of his systematic arrangement, the author has succeeded in presenting his subject in a complete and continuous manner without sacrificing the detailed consideration of the numerous constituent problems that together constitute the whole. The material is divided into short sections and paragraphs, each with subheads that indicate its content of subject matter. The argument is amply illustrated by tabular data, and copious references to the international literature are made.

The book is primarily academic and not clinical in nature. However, the distinct separation of fact and theory, the extensive use of illustrative experimental data, and the systematic arrangement, which facilitates reference, should make it a valuable addition to the library of the well informed physician as well as to that of the biologist.

Housing and the Community—Home Repair and Remodeling. Reports of the Committees on Housing and the Community, Joseph H. Pratt, M.D., Chairman, Reconditioning, Remodeling, and Modernizing, Frederick M. Feiker, Chairman. Edited by John M. Gries and James Ford. Publication No. 9 of the President's Conference on Home Building and Home Ownership. Cloth. Price, $1.15. Pp. 291, with illustrations. Washington, D. C.: President's Conference on Home Building and Home Ownership.

This is a careful study of housing, home repair and remodeling, with special reference to the relation of housing to health, delinquency, industrial efficiency, safety, citizenship, recreation and education. There is an extensive bibliography with many quotations and abstracts referring especially to housing and crime. The committee displays a praiseworthy caution in drawing conclusions as to the causative relationship between bad housing and bad health, delinquency, industrial inefficiency and crime. The book does point out that bad housing is almost universally related to other unfavorable environmental influences and that it is probably one factor in creating or at least favoring the increase in social maladjustment. It points out the importance of wise financing and planning of housing developments. The book is a storehouse of facts and the conclusions are in most instances sufficiently guarded to indicate that, while a strong impression exists that bad housing is bad municipal economy, there is no statistical proof. Perhaps impressions are worth more than statistics in arriving at such a judgment. Particularly valuable is the appendix, which contains a home inspection check list, by means of which a building can be evaluated by the occupant or prospective purchaser as to its desirability for a home with respect to construction, safety, health convenience, equipment, fire hazards and probable future value. This is a reference book which every health and social worker needs to read.

Verhandlungen der Deutschen Gesellschaft für Kreislaufforschung. VI. Tagung, gehalten zu Würzburg am 6. und 7. März 1933. Herausgegeben von Prof. Dr. Bruno Kisch. Paper. Price, 15 marks. Pp. 276, with 132 illustrations. Dresden & Leipzig: Verlag von Theodor Steinkopff, 1933.

There are altogether twenty-eight papers in this volume of transactions. In addition there are numerous discussions, some of which are evidently reported in full. The general subject of the meeting was the circulation and the nervous system. The leading paper ("referat"), taking up particularly the anatomic and physiologic aspects, was by H. E. Hering of Cologne. The leading paper dealing with the clinical features was by F. Kauffmann of Berlin. Among the papers were several dealing with the carotid sinus, a few with the electrocardiogram and with cardiac irregularities. Various phases of blood pressure were also discussed. The president of the society, Professor E. Magnus-Alsleben of Würzburg, delivered the opening address, which was largely historical. The volume is useful for reference and is of especial interest to one wishing to know the latest views of our German colleagues on a subject that the president said had been regarded by some as too difficult to be taken up, a fear, however, which he did not share.

The 1933 Year Book of Radiology, Diagnosis. Edited by Charles A. Waters, M.D., Associate in Roentgenology, Johns Hopkins University. Therapeutics. Edited by Ira I. Kaplan, B.Sc., M.D., Director, Division of Cancer, Department of Hospitals, City of New York. Cloth. Price, $7. Pp. 804, with 780 illustrations. Chicago: Year Book Publishers, Inc., 1933.

In this collective review of the year's progress in radiation diagnosis and therapy, the authors have excelled their effort of last year to present a readable, well arranged, sufficiently illustrated summary of recent progress in their respective fields. It would seem to be an indispensable volume for every radiologist, and it will be of assistance to every physician who desires to keep abreast of radiologic progress. The attention devoted to foreign literature is gratifyingly increased over the space given to foreign abstracts in the previous volume. Methods employed in radiation therapy are constantly being revised, and irradiation is being called on increasingly for the treatment of an ever-growing number of complaints. The field of radiologic physiology, biology and physics still constitutes a challenge to research for the elucidation of many unknown factors. It is apparent that biologic functions play a more important part than the mere physical variations in the rays produced by voltages of different amount, or by the gamma rays of radium. Additional experience tends to show that longer exposures, perhaps amounting in some selected cases to the whole-body irradiation method of Heublein, are preferable to the shorter more intense, more localized, treatments. It is hoped that the authors may receive sufficient encouragement in their work to insure the annual reappearance of this volume.

Diagnostik und Therapie der Lungen- und Kehlkopftuberkulose. Von Dr. H. Ulrici, Arzti. Direktor des Tuberkulosekrankenhauses der Stadt Berlin in Sommerfeld (Osthavelland). Second edition. Paper. Price, 25 marks. Pp. 389, with 269 illustrations. Berlin: Julius Springer, 1933.

The subject of tuberculosis, like the politics of the day, is undergoing a rapid and striking change and the present edition is practically a new book. After thirty-five pages devoted to pathogenesis and pathology, similar space is allotted to childhood tuberculosis. Physical, radiologic and bacteriologic diagnosis is well discussed. The exudative and productive types of pulmonary tuberculosis as well as hematogenous tuberculosis are described. To treatment, 100 pages is assigned. Specific therapy, chemotherapy and complications have ample sections given them. Laryngeal tuberculosis is discussed satisfactorily in seventeen pages. The section on intestinal tuberculosis is not satisfactory. The psychology of the consumptive is fully discussed. The use of alcohol in treatment is mentioned, and one learns that the author does not advocate its use except for the usual extreme conditions. The Gerson-Sauerbruch-Hermannsdorfer diet is given, and some discussion of gold treatment, to which Ulrici is neutral or mildly opposed. It is interesting to note that he advocates roentgen treatment of forms of productive tuberculosis which are tending to induration. There is no mention of the use of Bacillus Calmette-Guérin. A good discussion of surgical measures occupies the last third of the book. It is to be noted that Ulrici does not favor phrenic exeresis but rather emphraxis. There are new sections on oleothorax and on plombierung. The book is a good summary of modern German work on tuberculosis and is written in a clear style and well printed. The numerous illustrations are admirable, far better than those usually issued by American publishers. The bibliography is practically all German, for only two references are given to foreign literature, one American, one French. In spite of this the author has not overlooked much and to all who read German the book is heartily recommended, for one is impressed by the scientific manner in which the author gives his own experience in sections where his is at variance with that of others.

Histopathology of the Peripheral and Central Nervous System. By George B. Hassin, M.D., Professor of Neurology, University of Illinois College of Medicine. Cloth. Price, $4. Pp. 491, with 229 illustrations. Baltimore: William Wood & Company, 1933.

This textbook is by far the best that has appeared in the recent deluge of works on neuropathology. It is written by a man who has had great clinical experience and possesses an intimate first-hand knowledge of preparations of pathologic material and of the methods by which these preparations were obtained. Although written in a style that sometimes differs from the American idiom, the descriptions of the microscopic slides are so objective that one has the impression that the author wrote them directly from the slides. The illustrations, particularly the photomicrographs, are excellent, and the publishers have done a worth-while job in reproducing them—in fact, the illustrations are much better than one usually finds in a textbook for students. Hassin has several radical theories; for example, that the choroid plexuses, instead of secreting cerebrospinal fluid, absorb it. Although he has paid too little attention to experimental evidence and lays too great stress on doubtful pathologic material, in this book he has refrained from emphasizing his radical point of view and on the whole his summaries of disease entities will be clearly understood by the student. The book has perhaps only one fault, which will probably always be found in a pathology written by a clinician: that not enough space is given to the fundamental disease processes and too much space is given to the diagnostic characteristics of all the different diseases. The first part deals with the diseases of the peripheral nerves, the second part with the diseases of the spinal cord, the third part with the diseases of

the brain, and the fourth part (a welcome addition) with the most useful staining methods that are applicable to nervous material obtainable in the routine pathologic laboratory. Hassin's book deserves an enthusiastic reception.

Die Epidemiologie des Typhus abdominalis unter besonderer Berücksichtigung des Bact. typhi flavum. Von Prof. Dr. med. et phil. E. G. Dresel, Direktor des Hygiene-Institutes Greifswald. Heft 1, Mikrobiologie, Immunbiologie und Grenzgebiete. Wissenschaftliche Zeitfragen. Paper. Price, 3.60 marks. Pp. 40, with 2 illustrations. Leipzig: Johann Ambrosius Barth, 1933.

German bacteriologists in and about Greifswald have been interested recently in a yellow variant of the typhoid bacillus ("Bacterium typhi-flavum"), which they believe to be "a more or less saprophytic form" capable of longer life outside the human body than the ordinary typhoid bacillus. In Dresel's opinion the occurrence of this resistant type explains some allegedly obscure facts in the epidemiology of typhoid. It may be questioned whether the sources of infection of typhoid are in reality as confusing as they are assumed to be in this pamphlet.

Nervous Breakdown: Its Cause and Cure. By W. Béran Wolfe, M.D., Director, the Community Church Mental Hygiene Clinic, N. Y. Cloth. Price, $2.50. Pp. 240. New York: Farrar & Rinehart, Inc., 1933.

Psychiatrists seldom use the term "nervous breakdown." The public uses it constantly. So Dr. Wolfe has written a book on psychoneurotic reactions for the public in words it can understand. He is a sympathetic follower of much of what Dr. Alfred Adler has taught. The author's explanation of the "nervous breakdown" as "a valuable unconscious offensive-defensive device designed to save 'face' before personality disaster occurs" will not fit all cases but is accurate in enough instances to justify amply the text that follows. The seven chapters are on causes, symptoms, cases and cures (three chapters), plain words to patients, and creative self realization. The book is exceedingly well written, contains a fund of excellent advice, is well balanced in its scientific outlook and is distinctly practical. It shows ample evidence of orderly thinking and presents suggestions in a common sense and usable fashion. It can be unreservedly recommended to the layman.

Les arthrodèses dans la coxalgie: Indications, technique, résultats éloignés. Par Paul Bufnoir. Préface du Professeur Sorrel. Paper. Price, 20 francs. Pp. 109, with 9 illustrations. Paris: Masson & Cie, 1933.

The author describes the indications, contraindications, general principles, complications, technic and end results in cases of tuberculous hip disease treated by arthrodesis. He reports twenty-nine old cases occurring in adults. He describes eight old cases of arthrodesis for tuberculosis of the hip in the process of evolution in infants. The illustrations are well reproduced.

Bone Growth in Health and Disease: The Biological Principles Underlying the Clinical, Radiological, and Histological Diagnosis of Perversions of Growth and Disease in the Skeleton. By H. A. Harris, D.Sc., M.B., B.S., Professor of Clinical Anatomy, University College and University College Hospital, London. Cloth. Price, $10.50. Pp. 248, with 201 illustrations. New York & London: Oxford University Press, 1933.

This book is the outgrowth of articles published in such periodicals as the *British Journal of Radiology*, the *Journal of Anatomy* and the *Lancet*. Those who have read the original articles will be glad to see them in book form. The author, who is an authority on the subject, offers a wealth of material in presentable form. The book is divided into three parts, on lines of arrested growth in the long bones in childhood, bone growth with special reference to deficiency diseases, and significance of the fundamental processes of growth and repair in skeletal disease. First are recorded clinical and experimental researches on the growth of bone. In the first part the researches are based on a study of arrested growth in disease and in experimental animals. The author indicates the application of the results of this study to the elucidation of certain clinical facts in diseases of children and animals, and this forms the main portion of the second part, with special reference to the correlation of roentgenographic appearance and histologic structure. The third part contains recent investigations in which Harris demonstrates the distribution of mitotic zones in cartilage. The distribution of glycogen in relation to phosphatase and the reversion to primitive morphologic character that accompany the age changes in the skeleton are but an index of the work to be pursued in the future. The author states that the romance of bone growth is not yet exhausted. The manifestation of disease in bone, the registration of lines of arrested growth in the long bones, the phenomenal response of certain deficiency diseases to vitamins, the age changes in bone, and the extent to which the child can "grow out of" disease conditions, still present fundamental problems in clinical research and biology. The illustrations, including line drawings, reproductions of photographs and roentgenograms, gross sections and microscopic sections, are instructive and beautifully reproduced. The author's experimental work is given and a good bibliography is appended. This book should be of interest to every pediatrician and orthopedic surgeon.

Medicolegal

Malpractice: Abandonment of Patient After Operation.—The plaintiff sued the defendant-osteopaths for malpractice. He charged: (1) that they had erroneously diagnosed his condition as appendicitis and had performed a useless operation, (2) that they so carelessly and negligently performed the appendectomy as to cause a stoppage or obstruction in his bowels, and (3) that they failed to render him the proper postoperative care. At the close of the plaintiff's evidence, the trial court ruled that the evidence was insufficient to justify the submission of the case to the jury. Subsequently, on appropriate motion by the plaintiff, the trial court revised its ruling and ordered the defendants to stand trial on the charge of negligent postoperative care. From this revised ruling the defendant Laughlin appealed to the Supreme Court of Missouri, division 1. The evidence, said the Supreme Court, must be viewed in the light most favorable to the plaintiff. Briefly, the plaintiff, Aug. 28, 1928, consulted Sites, an osteopath, for relief from a severe pain in his abdomen. Sites diagnosed the ailment as appendicitis and advised an immediate operation, which was performed by Laughlin, another osteopath. After the operation the plaintiff began vomiting and continuously suffered intense pain in his abdomen, which was "swollen as tight as a drum." He remained in the hospital thirteen days, during which time he had no bowel movement and vomited fecal matter "every day or so." He complained to interns and nurses and asked that Laughlin be called but the latter did not appear. Apparently nothing was done during his stay in the hospital to relieve the plaintiff's condition. On September 10 he was discharged from the hospital and returned to his home, where Sites continued to treat him. Five days later, his condition becoming worse, a nonsectarian practitioner was summoned and a diagnosis of intestinal obstruction was made. Finally a passage of the bowels was induced, September 29, the thirty-first day after the operation.

In the absence of an agreement, understanding or notice to the contrary, said the Supreme Court, when a physician is employed to perform an operation, the relation of physician and patient continues until ended by the mutual consent of the parties, or by the physician's withdrawal after reasonable notice, or by the dismissal of the physician by the patient, or by the cessation of the necessity that gave rise to the relation. The physician must not only use reasonable and ordinary care and skill in performing the operation but during the continuance of the relation of physician and patient he must exercise ordinary diligence in the subsequent treatment. He must give, or see that the patient is given, such attention as the necessity of the case demands. Laughlin, continued the Supreme Court, was in charge of the case from the time the plaintiff entered the hospital and during the time he remained there. There was no agreement limiting his service to the mere performance of an operation or any agreement, understanding or notice to the plaintiff that Laughlin would not thereafter either attend and treat the plaintiff or see that such proper care and treatment as the case might require were received. The plaintiff placed himself in Laughlin's hands, submitting to and relying on his knowledge, skill and judgment. After the operation the plaintiff remained under Laughlin's care, relying on his judgment, and the relation of physician and patient continued.

Laughlin contended that the question whether or not requisite degree of care and skill were exercised in treating the plaintiff is to be tested by the general rules and principles of osteopathy, not by the principles of nonsectarian medicine. This argument, said the Supreme Court, has no application to the facts presented here, for the plaintiff's action does not proceed on the theory that some improper method, system or course of treatment was used, but that after the operation Laughlin negligently failed to discover and observe the plaintiff's condition and symptoms and negligently failed to give, or cause to be given, the attention and care which such condition demanded. The intestinal obstruction that developed immediately after the appendectomy continued to grow worse. The distended abdomen, the intense suffering, the absence of any bowel movement, and the vomiting of fecal matter should have indicated a serious intestinal obstruction. It is apparent that this condition was such as to have been readily discoverable by the exercise of that reasonable degree of care, examination and attention which it was incumbent on Laughlin, as the physician in charge of the case, to exercise. The plaintiff's evidence, concluded the court, was sufficient to justify submission of the case to the jury to determine whether or not Laughlin negligently failed to exercise reasonable care toward the plaintiff after the operation and whether the alleged nonattention and failure to observe and discover his condition and administer or give treatment calculated to correct or relieve such condition proximately contributed to aggravate, intensify and prolong the plaintiff's ailment. The action of the trial court in awarding a new trial to the plaintiff was accordingly affirmed.—*Reed v. Laughlin (Mo.), 58 S. W. (2d) 440.*

Malpractice: Gangrene Following Treatment of Fracture.—The plaintiff, a girl 12 years old, fell from a swing and broke both bones of her left arm, just above the wrist. The ends of the bones extended through the skin and became covered with dirt. She was taken to a hospital and there placed under the care of the defendant-physician. Two days thereafter gangrene set in and on August 16 it became necessary to remove the arm at the shoulder. An uneventful recovery followed. In this suit against the defendant for malpractice, the plaintiff claimed that the defendant was negligent in rendering treatment in the first instance, in that he used dry dressings, when he should have used wet; and that, while he dressed the arm on the morning of August 15, he did not again see the patient until he was called by the supervisor of nurses at the hospital, about 6 a. m., August 16, and that no other competent persons examined the patient in the meantime. The trial court gave judgment for the plaintiff, and the defendant appealed to the Supreme Court of Alabama.

It was claimed that on the afternoon of August 15, manifest signs of the infection were in evidence, which would have been discovered by the defendant had he examined her that afternoon or night. The defendant contended that he did examine the patient several times, and the hospital chart showed that he made an examination on the afternoon of August 15. There was, however, substantial evidence to the contrary. The expert witnesses were in accord, said the Supreme Court of Alabama, that the circumstances of the accident, known to the defendant, suggested the probabilities of gangrene, known to be very dangerous. Such knowledge, all admitted by the defendant, demanded frequent examination and radical treatment. There was substantial evidence that on the afternoon of August 15 the wound emitted a strong and offensive odor and that the patient had fever and was restless. Early the following morning the infection had extended past the elbow. That circumstance and the evidence of the symptoms on the preceding afternoon and night justify an inference that the infection on that afternoon could and would have been detected by a competent person, said the court, and prompt and efficient treatment would have probably stopped its progress and prevented the necessity of amputation. When a physician undertakes to treat a patient whose condition, known to the physician, is such that without continuous or frequent expert attention injurious consequences may result, he must either render such attention himself or see that some other competent person does so. The question of the defendant's negligence was a fair issue for the jury. The trial court, however, refused to charge the jury that if they believed the evidence they could not find for the plaintiff because the defendant used dry bandage in dressing the plaintiff's injury. This was error, said the Supreme Court. The gravamen of the complaint is negligence, not want of skill. Where there are various recognized methods of treatment, the physician is at liberty to follow the one he thinks best and is not liable for malpractice because expert witnesses give their opinion that some other method would have been preferable. The experts in this case all agreed that wet and dry dressings in such cases are both used by skilful physicians and that standard authorities approve them both. It is largely in the sound discretion of the surgeon in charge of the case. The defendant was shown to have been a competent surgeon and used the method adopted by him with care and skill, and the wound continued to drain to the last and did not seal up. This is the result the best process was expected to secure. For using dry bandage, the defendant is not chargeable with want of due care, or negligence, and the refusal of the trial court to charge the jury as requested constituted a prejudicial error to the defendant. The judgment of the trial court, therefore, was reversed and the case remanded.—*Jackson v. Burton (Ala.), 147 So. 414.*

Society Proceedings

COMING MEETINGS

American Academy of Orthopedic Surgeons, Chicago, Jan. 8-10. Dr. Philip Lewin, 104 South Michigan Blvd., Chicago, Secretary.

Annual Congress on Medical Education and Licensure, Chicago, February 12-13. Dr. W. D. Cutter, 535 North Dearborn Street, Chicago, Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH

Sixth Annual Meeting, held in Chicago, Oct. 27 and 28, 1933

(Concluded from page 2078)

Studies on Surgery of the Inferior Vena Cava

DRS. WALTMAN WALTERS and JAMES T. PRIESTLEY, Rochester, Minn.: Experimental and clinical studies were made following incision and suture of the inferior vena cava. In the experimental studies on dogs, a portion of the vena cava was removed and the vessel repaired with specially prepared silk sutures. Subsequently, at varying intervals, necropsy was performed on the dogs to ascertain the status of the healing processes in the vena cava and to discover any possible evidence of thrombosis or embolism. Serial microscopic preparations made from the vena cava at the operative site evidenced the reparative reaction in the wall of the vein, starting with early fibroblastic proliferation in the adventitia and ending with complete endothelization of the intimal layer. In four clinical cases the inferior vena cava was opened for the removal of papillary projections of a right renal neoplasm, or during mobilization of a densely adherent kidney. In each case hemostasis was satisfactorily obtained, by suture in some cases and by the application of hemostats in others, without the necessity of ligating the vena cava.

DISCUSSION

DR. MORRIS H. NATHANSON, Minneapolis: I should like to ask concerning the possibility of operating on the inferior vena cava within the pericardium. Several years ago I reported some cases of therapeutic pneumocardium before this society. In one case the air did not appear on the right side of the heart, which indicated that there were some adhesions in this region. The patient later developed a cardiac decompensation with only slight dyspnea but marked liver enlargement and ascites. I considered that this might be due to adhesions about the inferior vena cava and this was found at autopsy. Were the possibilities good for surgical intervention in this case?

DR. ARGO J. BEEM, Cleveland: I should like to ask the authors whether they have had evidence of thrombosis.

DR. J. T. PRIESTLEY, Rochester, Minn.: I have had no experience with clinical surgery of the vena cava for adhesions

about the pericardium. In animals the vessel can be approached quite satisfactorily and can be manipulated with a certain amount of success and satisfaction, in this region. Very few satisfactory results following pulmonary embolectomy have been reported. If conditions are favorable, the vena cava might possibly be operated on at that point. I endeavored to discuss the evidence of healing in the vena cava and to discover any possible evidence of thrombosis or embolism. No pulmonary emboli were discovered in any animal; however, in several instances there was a small adherent thrombus at the operative site.

Focal Infection and Erythema Nodosum

DR. ISADORE PILOT, Chicago: Erythema nodosum was observed as a sequela of streptococcic sore throat in which filtrates of the hemolytic streptococci produced typical nodules on intradermal injection. Tuberculin tests in two patients gave no reaction. In another rare type of case, erythema nodosum complicated lymphogranuloma inguinale. The Frei test was positive, and the lesion from the intradermal test was markedly nodular. A third common type gave a nodular reaction to tuberculin. In the two latter instances, streptococcus filtrate caused no reaction. It would appear that erythema nodosum is not a clinical entity but a peculiar hypersensitive response of the skin to toxic products from foci of infection due to streptococci, tubercle bacilli, the virus of lymphogranuloma inguinale and perhaps other agents.

DISCUSSION

DR. H. M. CONNER, Rochester, Minn.: I should like to ask Dr. Pilot whether he considers these reactions sufficiently definite, so that, given a case of erythema nodosum, one could, by use of a series of antigens, decide on the etiologic agent.

DR. ISADORE PILOT, Chicago: These reactions were not of the immediate allergic type that one sees with proteins. They come on in twenty-four hours and instead of fading, as in connection with the tuberculin test, they go through an involution as an erythema nodosum nodule and persist up to ten days. I have tried other streptococcus antigens, for instance, the scarlet fever streptococcus. This will give an inflammatory reaction, but the nodule is not as violent or as marked in its extent as the nodule from the autogenous strain. As far as treatment is concerned, there is nothing to do in these cases. When the streptococci disappear from the throat, the focus apparently is of only transitory nature and the erythema nodosum disappears. In one instance, although the erythema nodosum cleared up the arthritic pains persisted. About four months later the tonsils were removed and the same streptococci isolated. The arthritic pain that had been present disappeared, so the tonsils could be considered the focus. In using tuberculin, one should employ 1:10,000 instead of 1:1,000. With reference to streptococcus antigens, one can obtain some definite reaction with stock antigens of hemolytic or even nonhemolytic type, but it is preferable to make the antigen from the patient's own throat if there is a definite history or definite evidence of a focus.

Measurements of Muscular Work in Occlusive Arterial Disease of the Lower Extremities

DRS. DWIGHT L. WILBUR and GEORGE E. BROWN, Rochester, Minn.: An attempt has been made to develop an apparatus with which the movement of walking is simulated in order that measurements of muscular work may be made on the basis of horse power units. In this way the extent of incapacity of patients with occlusive arterial disease and intermittent claudication, and the effects of therapy on them, can be determined. The apparatus consists of a sewing machine modified so that the patient's leg must push against a weight, which may be adjusted; by noting the duration of the experiment, the horse power that is developed can be measured. By this method the muscular capacity of the legs of twenty-nine normal persons who served as controls and those of thirty patients with various types of peripheral arterial diseases has been measured. The method is of value and with modifications, which come with experience, should be an adjunct in the study and treatment of patients with localized forms of arterial diseases. Errors inherent in this type of study are those of personal threshold of pain and fatigue, the factor of muscle conditioning, and unknown influences of the general state of the patient. Fairly close approximations of the amounts of muscular work can be obtained on repeated tests under variable conditions in normal and diseased subjects. The following results have been obtained: 1. As a group, those with occlusive arterial disease (thrombo-angiitis and arteriosclerosis obliterans) of the lower extremities are unable to perform as much work with their legs as do normal persons, and the degree of disability is quite similar in the two types of arterial disease. It follows, therefore, that the disability is dependent on occlusion rather than on the type of disease underlying the occlusive process. 2. In the normal and diseased subjects as groups the time of onset of the sensation of fatigue in the calf muscles was very much the same, but the duration of the exercise was sharply different. 3. No correlation could be established between the amount of muscular work performed and the severity of arterial occlusion of an extremity as demonstrated by the presence of pulsations of the arteries of the extremity and the grade of vasospasm as measured by dilatation with fever. 4. In those cases in which intermittent claudication was reproduced, the duration of the exercise, the total amount of work performed, the time of onset of fatigue, and the pulsation of the arteries were significantly less when compared with the group in which occlusive arterial disease was present but in which intermittent claudication was not a distinct symptom.

DISCUSSION

DR. L. N. KATZ, Chicago: In a series of studies carried out in the laboratory, my associates and I have been able to show that there are a number of factors contributing to the production of pain in intermittent claudication, the most important factors being the amount of muscular work, circulatory stasis, and the available oxygen to the tissues. I should like to ask the authors whether the patients had a preliminary period of rest before performing the exercise. We have found quite consistently, and contrary to the previous observations of Lewis, that a period of ischemia preceding the exercise will materially shorten the amount of exercise necessary to produce pain. I should also like to ask whether an attempt was made to evaluate the rôle of circulatory disturbances in venous flow, particularly those due to varicosities. We have found that venous stasis alone, without arterial occlusion, may lead to the development of pain on exercising the limb. Finally, I should like to ask whether an attempt was made to check the rate at which the exercise was performed by the patients. It has been clearly established that a given quantity of work may require a different amount of muscular effort, depending on the rate at which the movements are performed.

DR. DWIGHT L. WILBUR, Rochester, Minn.: Most of our patients were rested for a period of from ten to fifteen minutes preceding the test. It did not seem probable that moderate exercise just preceding the test had any great influence on the results of the exercise. Venous stasis was not present to a recognizable degree in the majority of our patients. Varicosities were uncommon. We considered the rate at which the machine was run and found it to be significant in regard to the horsepower developed but not as regards the total amount of work done. As a group, the arteriosclerotic individuals ran the machine considerable faster than did normal individuals and patients with thrombo-angiitis obliterans.

Relationship Between Acid-Base Equilibrium and Bacterial Flora of the Stomach

LLOYD ARNOLD and MARION HOOD, Chicago: There are certain differences between the behavior of bacteria in contact with living cells and their behavior in test tubes. A study of in vivo bacteriology has opened up new fields. Several body surfaces have been studied, such as the skin, the oral and nasal cavities, the conjunctiva, the stomach, the small intestine and the vagina. Some observations dealing with the stomach are to be reported here. Arnold and Johnson found that the free acid gastric contents of dogs did not kill bacteria but exercised only a bacteriostatic influence on the flora. Continuous observations showed bacteria to be nonviable in the gastric lumen in the presence of free acid, but a heavy viable flora appeared at the time the free acid disappeared or was neutralized.

Arnold recorded certain bactericidal or self-disinfecting powers of the small intestine. There is a correlation between the bacterial flora of the stomach and the small intestine. Gastric studies were extended to human subjects. Cultures of fractional aspirations of fasting gastric contents were taken on plain agar plates and the hydrogen ion concentration was determined colorimetrically. The acid-base equilibrium was adjusted toward the acid as well as the alkaline ranges and the changes in endogenous bacterial flora were determined by agar cultures as well as direct smears. Hydrochloric, acetic and lactic acid solutions and lemon and orange juice were used as acidifying agents. There are definite correlations between the acid-base balance and viable bacteria in the gastric lumen. The experimental work reported on laboratory animals has been substantiated. Dr. Gulbrandsen from this laboratory has found a correlation between the acid-base balance of the duodenum and the bacterial flora of this region. Acid-reacting duodenal contents are usually sterile on culture; alkaline-reacting duodenal contents give heavy growths of bacteria by cultural methods. The development of knowledge of the bacterial flora residing within the lumen of the stomach and upper levels of the small intestine may indicate a new approach to certain metabolic disturbances associated with decreased gastric acid secretions. The possible influences of this intragastric bacteriostatic mechanism on the degenerative diseases of the older age groups has been outlined by Arnold.

Effect of Sphlanchnic Nerve Section on Carbohydrate Metabolism

DRS. G. K. FENN and GÉZA DE TAKÁTS, Chicago: An attempt has been made to stabilize the carbohydrate tolerance and to reduce materially the insulin requirement in the juvenile diabetic patient. This end has been sought by means of section of the sphanchnic nerves. One case (already reported) in which a rather striking result was achieved was in contrast to a second case, in which the result was much less striking. A method of case selection has been devised which may result in the separation of diabetic patients into different groups. The use of insulin sensitivity curves in normal persons and diabetic patients and the blood sugar responses to the ingestion of galactose before and after the administration of ergotamine constitutes a method of case separation that appears to be of value in the selection of cases for this type of treatment.

DISCUSSION

DR. RUSSELL M. WILDER, Rochester, Minn.: I regard these studies as of great importance. They bear on the heretofore ambiguous subject of sensitivity to insulin. But I am inclined to dispute the conclusion that different varieties of diabetes are indicated by these different reactivities to injections of insulin. I suspect rather that the test is a test of different kinds of people with the same disease and that the response obtained depends on the irritability of the nervous system.

DR. R. W. SCOTT, Cleveland: I should like to ask whether the authors made any observation on how these individuals tolerate the effect of gravity on the circulation.

DR. M. H. NATHANSON, Minneapolis: I am interested in the result obtained with ergotamine. The specific action of ergotamine is paralysis of the sympathetic nerve endings. In some studies which I am carrying out I attempted to modify the effect of epinephrine on the cardiac mechanism with ergotamine. I found, however, that I could not give doses sufficiently large in human beings to paralyze the effect of epinephrine on the heart. When one inspects the pharmacologic literature, one finds that the doses of ergotamine used to antagonize the pressor effect of epinephrine in the experimental animal are much larger than those which are used in man. It is interesting, therefore, to see that there is some modification of sensitiveness to insulin in man with moderate doses of ergotamine.

DR. E. L. SEVRINGHAUS, Madison, Wis.: It is rather noticeable that among juvenile diabetic patients there are occasionally young men and young women that are difficult to manage over a long period because of sudden shifts in glycemia. Erratic hyperglycemia properly leads these patients to increased doses of insulin. Hypoglycemic reactions of severe types frequently follow. These patients seem to be emotionally unstable also. I wonder whether the authors have any data as to whether these patients that are more easily stabilized after splanchnic section are among those who are emotionally unstable; also whether they have any observations on change in the sympathetic mechanism after splanchnic section and whether it has any effect other than on the carbohydrate metabolism, such as on the responses to emotional stimuli.

DR. GÉZA DE TAKÁTS, Chicago: It is obviously more difficult to suppress the pressor effect of epinephrine with ergot than the hyperglycemic effect. It is also true, of course, that much smaller quantities of epinephrine are necessary to produce hyperglycemia than to produce the rise in the blood pressure. The flattening of the hyperglycemia curve after the administration of ergotamine may be an inhibition of the sympathicosuprarenal mechanism, but it also may be due to an increased utilization of sugar in the periphery. Our present data do not supply any information on this question. In reply to Dr. Sevringhaus I may state that the splanchnic section did stabilize tolerance in the first case, in which two respiratory infections were not followed by decrease in tolerance. In the second case we had no such experience. In regard to Dr. Scott's question, the effect of gravity on blood pressure following splanchnic section was quite marked for about four weeks after both operations. The systolic pressure dropped from 100 to 85 and as low as 75 mm. of mercury after three or four minutes of erect posture. However, after from four to six weeks neither of the two patients showed this postural hypotonia. Regarding Dr. Wilder's question, it may be not that the types of diabetes are different but that the same type showed different manifestations in different types of constitutions. Nevertheless, an increased sympathetic irritability of the glycosecretory mechanism may be beneficially affected by the suppression of such nervous impulses. The operation, as we see it now, seems worthy of trial in juvenile diabetic patients who are insulin resistant and respond well to ergot.

Special Features of the Epidemic of Encephalitis in the St. Louis Area

DRS. G. O. BROUN, R. O. MUETHER, MAURICE W. SBERTOLI and A. F. DEL VALLE, St. Louis: The average case was characterized by sudden onset with headache, muscular aches and sometimes chills, and by high irregular fever usually of seven to fourteen days' duration terminating by lysis. Meningeal symptoms, such as headache, drowsiness, stupor, mental confusion and delirium, predominated. Cranial nerve palsies were relatively rare. Neck rigidity, muscular tremors and spasticity, positive toe signs, absent or unequal tendon, abdominal and cremasteric reflexes were the most common physical observations. Some evidences of myocardial weakness were often noted in severe cases. Respiratory symptoms other than terminal pneumonia rarely occurred. Nausea and vomiting were frequent. The urine occasionally contained albumin, pus, erythrocytes and casts. Some elevation of blood nonprotein nitrogen was not infrequent. Blood sugar tended to be slightly increased, but glycosuria was very rare. Moderate polymorphonuclear leukocytosis was present in the majority of cases. The spinal fluid was clear, with usually some increase in pressure, a positive globulin, a normal sugar content, and an increased count of lymphocytic cells. The colloidal gold showed a tabetic curve. Convalescence was usually rapid, with few immediate serious nervous sequelae. The mortality was low in patients under 40 years of age. It was especially high in cases showing preexisting morbid conditions, particularly hypertensive vascular disease.

Pathologic Changes in Patients Dying of Encephalitis

DRS. R. S. MUCKENFUSS and H. A. MCCORDOCK, St. Louis: The most interesting pathologic lesions characteristic of the various types of encephalitis and the lesions found post mortem in patients dying in the present epidemic were found in the kidneys, which were swollen and intensely congested, the pelvis being studded with small hemorrhages. Intramuscular inclusion bodies were found in the cells of the tubules by Dr. Margaret Smith in about 50 per cent of the cases so far studied.

DISCUSSION ON ENCEPHALITIS

DR. M. A. BLANKENHORN, Cleveland: I should like to ask whether the pulmonary changes and kidney lesions can be considered in any way complications or are they secondary infections?

DR. H. M. CONNER, Rochester, Minn.: Has there been any attempt at the production of the disease in animals and if so, with what success? Also, I should like to ask whether or not the inclusion bodies in the kidneys have any significance.

DR. C. F. KEMPF, Indianapolis: I had an opportunity of seeing cases in Indianapolis during the epidemic of encephalitis that appeared in 1929, 1930 and 1931. Clinically this group of cases, of which there were something like 260, is very similar to the clinical picture described by Dr. Broun and his associates. I doubt whether from the clinical observations one could tell the difference. There were a few mild cases, but the greater proportion terminated fatally in a very short time. There were more signs of meningeal irritation, and a greater number of these cases showed delirium. In the spinal fluid more cases presented a low cell count than an increased count. The colloidal gold changes were rather similar. However, intraspinal drainage was continued in many of these cases for several weeks. The greatest difference in the two epidemics was in the pathology. The cases seen in Indianapolis either showed nothing more than a dilatation of the blood vessels, with some damage to the cortical cells, or some very definite meningeal changes without any perivascular areas or very few areas of focal necrosis. The virus was not demonstrated. Certainly the conditions clinically are very similar.

DR. G. O. BROUN, St. Louis: The clinical picture presented was not sufficiently specific in itself to permit of absolute diagnosis. In the group that we studied there were a number of cases originally diagnosed as encephalitis that did not show it. I will mention one case specifically. The history and physical observations, if compared with those in many cases of encephalitis, were practically identical. There were headache, fever, nausea, vomiting, somnolence, slight rigidity of the neck, inequality of the reflexes, and one or two positive toe signs. The spinal fluid was clear, with a cell count of 52, and normal spinal fluid sugar. It proved to be a case of typhoid. Another patient came in with headache, neck rigidity, and a spinal fluid cell count of 30. Very quickly after admission the patient was found to be suffering from malaria and on the administration of quinine the symptoms cleared up. I think it must be remembered that there is probably some increase in the spinal fluid cell count in many acute febrile diseases as well as in encephalitis. This means that every case must have a bacteriologic study before the diagnosis can be established with certainty. Regarding the colloidal gold curve, we usually made two spinal fluid examinations, one at the time of admission and one at the time of discharge. Ninety per cent of the colloidal gold tests showed a tabetic curve on admission and most of them showed the same on discharge. If there is any change, it usually is a flattening out of the curve. We had one or two with a paretic curve and a few more with a normal curve. The cell count was still somewhat high in convalescents, many cases showing counts of from 10 to 30.

DR. R. S. MUCKENFUSS, St. Louis: I am not able to say definitely whether the changes in the lungs and in the kidneys were actually part of the disease picture or were complications. They undoubtedly occurred in quite a high percentage of the cases. It is probable that they were in some way associated with the disease, but we have no direct proof of this. As to the inoculation of animals, numerous attempts were made from the onset of the epidemic to determine the etiologic agent. Routine blood cultures and spinal fluid cultures were made. Because of the difficulty in some cases in distinguishing it clinically from typhoid, many stool cultures were made. With a few exceptions these were negative. When positive cultures were obtained, the variety and paucity of organisms were such that we felt that we were dealing with contaminants. Of the animals inoculated, manifestations similar to disease seen in man were observed in our laboratory in monkeys. These monkeys showed an elevation of temperature associated with some incoordination and tremors. The disease was passed from monkey to monkey with some difficulty. During this time we were sending autopsy material to a number of different laboratories. The material sent to Dr. Webster at the Rockefeller Institute was used in a strain of mice highly susceptible to neurotropic viruses. He was able to produce a disease that could be maintained in these animals. Accordingly, mice were inoculated from second passage monkeys, and a disease similar to that seen by Dr. Webster was established in stock mice. The identity of this virus has not been settled, but studies are in progress. We are exchanging strains of virus with Dr. Webster and these will be compared in both laboratories.

The Electrocardiogram in Myocardial Infarctions: A Review of 107 Clinical Cases and 108 Cases Proved at Necropsy

DR. A. R. BARNES, Rochester, Minn.: This study had three primary objects in view: 1. To furnish an answer to the question of whether or not other cardiac lesions produce electrocardiographic changes which duplicate the characteristic electrocardiographic picture of acute coronary occlusion. 2. To reexamine the value of the RS-T changes in the electrocardiogram following acute myocardial infarction as a means of predicting the situation of infarction before death. 3. To determine, in those cases in which electrocardiographic evidence of acute myocardial infarction is lacking, the reasons for this failure. Study of cases encountered at the Mayo Clinic leads to the following conclusions: 1. No other cardiac lesion reproduces in its entirety the typical RS-T modifications of the electrocardiogram described as characteristic of acute myocardial infarction. 2. In no instance in which a typical T_1 or T_3 type of electrocardiographic change has developed have we failed to find myocardial infarction in the region anticipated. Failure to do so has meant either that the tracing was not typical or that sufficient study of the pathologic change in the predicted region of infarction has not been carried out. 3. A considerable number of infarctions are not signalized by the development of typical changes in the RS-T segment of the electrocardiogram. In our cases this failure was accounted for by one of the following causes: (*a*) Electrocardiograms were not obtained in sufficient number or in proper time relation to acute myocardial infarction. (*b*) There were multiple areas of acute myocardial infarction. (*c*) The presence of bundle-branch block obscured the electrocardiographic pattern of infarction. (*d*) Pericarditis or pericardial effusion modified the electrocardiographic changes. (*e*) The amplitude of the deflections in lead I or lead II was so small that the RS-T changes characteristic of infarction could not be recognized. (*f*) The tracing was obtained when a patient was dying.

The combined consideration of the RS-T and Q patterns yield more information regarding the presence of myocardial infarction than does the consideration of either pattern alone. Frequently the two patterns are equally indicative of infarction. Fairly commonly the RS-T segment changes are more typical of myocardial infarction than are the Q patterns. In a smaller number of patients the Q patterns are more typical of infarction than are the RS-T changes. There is a considerable group of patients in whom the RS-T changes indicate myocardial infarction when the Q patterns are entirely lacking. There is an occasional case in which the Q pattern is indicative of infarction when RS-T changes are absent.

In our cases the Q_1 type of electrocardiogram is found in association with infarction involving the apex and anterior portion of the left ventricle. The Q_3 type of electrocardiographic change is associated with infarction of the basal portion of the left ventricle.

The development of a highly characteristic T_1 or T_3 type of electrocardiographic change following acute coronary occlusion seems to indicate a better prognosis than does an atypical tracing. Typical T_1 or T_3 electrocardiograms were encountered six times as commonly as atypical electrocardiograms in the patients who recovered. In patients who died, atypical tracings predominated over typical tracings in a ratio of four to three. The atypical tracings usually were found to be associated with multiple infarctions, extensive single infarctions, or complicating pericarditis, any one of which obviously increases the gravity of the outlook.

In cases the reports of which have been published, as well as in our series, T_1 and T_3 types occur with about equal frequency.

This means that the posterior basal portion of the left ventricle is infarcted approximately as often as the anterior apical portion.

Effect of Theophylline Ethylenediamine on Cardiac Infarction Produced by Ligation of the Coronary Arteries in the Dog

DRS. W. M. FOWLER, H. M. HUERVITZ and FRED M. SMITH, Iowa City: In perfusion experiments on the isolated rabbit heart, theophylline ethylenediamine produced a far greater and more consistent increase in the rate of coronary flow than any other of the drugs that were studied. The action of theophylline ethylenediamine on the coronary circulation was further investigated through its effect on the size of the infarct produced by the ligation of a coronary artery in the dog. In the dogs receiving theophylline ethylenediamine there was a decided reduction in the size of the infarct as compared to that of the control series. Moreover, the infarct was more sharply demarcated and did not present the usual frayed-out appearance encountered in the untreated animals. These results indicate that this drug promotes the development of collateral circulation and thereby reduces the extent of the myocardial damage resulting from the ligation of a coronary vessel.

Cardiac Infarction: Its Subjective Symptoms in Relation to Its Pathologic Anatomy

DR. NATHAN S. DAVIS III, Chicago: There have been suggestions that the presence or absence of pain in cardiac infarction is related to the underlying pathologic anatomy. In an attempt to confirm or refute this theory, some seventy-five records from the Department of Pathology of Northwestern University Medical School have been studied. It appears that the pain of cardiac infarction, like that of angina of effort is due to relative ischemia of the myocardium more than to anything else; that complete ischemia of a limited area of the myocardium does not cause pain.

DISCUSSION ON HEART DISEASE

DR. L. N. KATZ, Chicago: In regard to Dr. Barnes's paper, a careful survey of the reported autopsy cases by Gilchrist and Ritchie failed to show any clear-cut correlation between the configuration of the electrocardiogram and the location of the infarct. This conclusion Wilson and his co-workers also arrived at from a survery of their autopsy cases. At Michael Reese Hospital, Drs. Hamburger, Priest, Saphir and I have examined thirty-four consecutive autopsy cases, in twenty-one of which electrocardiographic records were taken. We could not consistently locate the position of the infarcts in this series from the appearance of the electrocardiograms. Korey and I have recently injected alcohol into various regions of the dog's heart and found that the electrocardiographic changes produced are not related to the location of the injured area. Furthermore, it must be borne in mind that, as Dr. Bohning and I have recently shown, it is not always easy to fit the electrocardiogram into the T_1 or T_3 types. In regard to Dr. Davis's paper, in the study mentioned we could not correlate between angina pectoris and the nature of the infarct.

DR. WARREN B. COOKSEY, Detroit: For several years I have been interested in a group of cases in which small infarcts were suspected but in which the infarcts could not be proved clinically. During a study of serial electrocardiograms following coronary thrombosis, I was impressed by the occasional striking changes that occurred in both T_1 and T_3. In certain cases the T_1 became very sharp, of greater than normal amplitude and positively directed, whereas T_3 became deeply cove negative. Because of the striking character of these changes, I have been interested in the frequency with which they also occur in patients of coronary sclerotic age with suggestive symptoms but who have never had a gross infarction. I have followed sixty cases with but one autopsy to date. This patient was being operated on under gas when, because of deep cyanosis, he developed ventricular fibrillation and died. He had numerous small healed infarcts along the course of the left descending coronary. I should like very much to hear whether Dr. Barnes or Dr. Scott or Dr. Katz has encountered these changes.

DR. ROY W. SCOTT, Cleveland: These three papers present many aspects for discussion to those interested in heart disease. The paper of Dr. Fowler and his associates on the effect of theophylline ethylenediamine on the dog's coronary arteries raises the question as to how closely these results apply to man. It has been known for a long time that caffeine and its derivatives increase the coronary flow in the animal heart, but few carefully controlled observations have been made on man. The best of these, so far as I know, are the studies recently reported by Wayne and Laplace, who found that theophylline ethylenediamine, either by mouth or intravenously, increases the amount of exercise tolerated by patients with angina of effort. The clinical reputation of theophylline ethylenediamine as a coronary dilator is based largely on statements that its use over long periods diminishes the frequency and severity of the attacks. Such evidence is admittedly difficult to evaluate. Dr. Fowler and his associates mentioned that their animals receiving theophylline ethylenediamine for twenty-one days following coronary ligation showed smaller areas of infarction than did animals that did not receive the drug, and they ascribe their results solely to the effects of the drug. This conclusion would seem warranted were there not a considerable variation in the coronary circuit in normal dogs. Dr. Davis's paper illustrates the difficulties in correlating a clinical syndrome with anatomic observations. Proved cases of acute coronary thrombosis occur without pain. Recently I saw a patient with excruciating pain in the left elbow but not in the chest. One is reminded of a small group of individuals dying of myocardial insufficiency from coronary disease in whom chest pain may never be a conspicuous feature. I refer to those cases in which the coronary arteries appear to be slowly occluded, resulting in an extensive fibrosis of the ventricles.

DR. M. H. NATHANSON, Minneapolis: I have had an opportunity to observe under somewhat controlled conditions the possible effects of theobromine and theophylline compounds in clinical cases. These compounds are expensive and at our hospital it was found that the cost approximated $400 a month, owing to the freedom with which the interns and residents prescribed these substances. Several months ago it was decided that these compounds could be prescribed by only two members of the staff. In the outpatient department it was found that while many patients did as well when sodium nitrite was substituted, certain other patients returned and stated that there was a definite increase in the frequency of their anginal attacks when the theobromine compounds were discontinued.

DR. A. R. BARNES, Rochester, Minn.: I regret that time does not permit me to answer each of Dr. Katz's criticisms in detail. Detailed analysis of the cases reported by Gilchrist and Ritchie shows that such inconsistencies as they have called attention to can be explained on the basis of the facts that I listed in discussing the cases of acute myocardial infarction in which electrocardiographic evidence of that event was lacking. For the most part, Wilson and his co-workers corroborated our localization hypothesis. In the last issue of the British journal *Heart*, Dr. Wilson thought he had found a definite exception to this localization in a patient with a T_3 type of electrocardiogram. Subsequent careful pathologic study proved this not to be the case. Dr. Katz maintains that infarction in the anterior and in the posterior portion of the left ventricle of the dog gives an identical tracing. A review of the experimental work on the dog's heart does not support that contention. I should like to point out that it is important for all physicians to consider both the Q and T patterns in an attempt to diagnose acute myocardial infarction. There is no doubt in my mind that typical T_1 and T_3 patterns will localize myocardial infarction accurately, but the confirmation of that must be left to the future. I am confident that, in time, an agreement will be reached.

DR. NATHAN S. DAVIS III, Chicago: In replying to Dr. Katz's question, I would say that in some of these cases there was hemorrhagic infarction and no pain. In the series there were several cases in which no narrowing of more than one branch of the coronary artery is reported. There may be some sclerosis in other branches, but no narrowing was reported in the record. I might also state that in classifying these cases I considered those with pain and those without pain. Some patients had pain only in the arm and shoulder, others only epigastric pain. A history of that sort of pain was considered positive in making this classification.

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Diseases of Children, Chicago

46: 473-704 (Sept.) 1933

Physiology of Cerebral Activity in Children as a New Subject of Pediatric Investigation. N. I. Krasnogorski, Leningrad, U. S. S. R.—p. 473.

Acid-Base Balance of New-Born Infants: IV. Effect of Ingestion of Alkali on Acid-Base Balance of New-Born Infants. V. W. Lippard and Eleanor Marples, New York.—p. 495.

*Encephalitis as a Complication of Measles: Report of Thirteen Cases. M. G. Peterman and M. J. Fox, Milwaukee.—p. 512.

*Acute Pyothorax: Treatment of Children and Infants by Aspiration of Pus and Air Replacement; Preliminary Report. H. Bloch and P. L. Parrish, Brooklyn.—p. 518.

*Guanidine Intoxication: Complicating Factor in Certain Clinical Conditions in Children. A. S. Minot and Katharine Dodd, Nashville, Tenn.—p. 522.

Encephalitis and Measles.—Peterman and Fox studied thirteen cases of encephalitis complicating measles. The cases conform to the typical picture as reported in that in twelve the onset occurred between two and six days after the onset of the rash and in one in eight days. In all but one the encephalitis began with stupor or drowsiness, and in this case the onset was characterized by restlessness and convulsions. Eleven patients (two were not so examined) exhibited a polymorphonuclear leukocytosis ranging from 12,600 to 26,000 leukocytes per cubic millimeter even up to fifteen days after the onset. The percentage of polymorphonuclears ranged from 74 to 84. All fluids were clear and seven were under increased pressure. The cell count ranged from 5 to 380, of which from 40 to 98 per cent were lymphocytes. The globulin was positive in six of the eleven fluids so tested. The sugar ranged from 71 to 125 mg. per hundred cubic centimeters in the eight fluids so tested. The colloidal gold test was made on six fluids; in three it was negative, and in three positive. The authors propose three theories in the explanation of encephalitis complicating measles: (1) It is the result of a virus independent of measles, (2) it is an allergic or anaphylactic phenomenon or (3) it is a virus activated by the measles organism. On the basis of the remarkable consistency in the clinical picture and observations in most established cases of encephalitis complicating measles, viz., time of onset in relation to the rash, the fever, the drowsiness or convulsions, the polymorphonuclear leukocytosis, the pleocytosis and the increased sugar in the spinal fluid and the pathologic changes, the authors are inclined to believe that the condition is a clinical entity produced by some specific virus or organism.

Acute Pyothorax.—Bloch and Parrish treated by aspiration and air replacement fourteen infants and children having acute pyothorax following pneumonia. The apparatus consists of a 30 cc. Luer syringe and a large needle. Fairly certain location of the empyema should be made clinically and roentgenologically. The left thumb is pressed against the lower border of the upper rib, thus protecting the intercostal artery, vein and nerve. The needle is inserted through the intercostal space directly beneath the thumb. By the aspiration of pus, it is definitely ascertained that the needle is in the empyema cavity. A syringeful of pus is then removed and an equal amount of air is injected with the same syringe. This is repeated until on aspiration no pus enters the barrel. The injection of an additional 10 or 15 cc. of air will facilitate the aspiration of any remaining pus. Tappings are repeated every four to seven days.

Guanidine Intoxication.—The procedure that Minot and Dodd used for the determination of guanidine is essentially the earlier method described by Major and Weber with a few minor changes. The estimation was carried out on protein-free filtrates prepared from blood by the method of Folin and Wu. This filtrate contains the interfering salts and nonprotein extractives of blood and the guanidine in far too great dilution for colorimetric estimation. Before the color test is made, most of the salts are removed, creatine is converted to creatinine and the guanidine concentrated in a small volume of solution. In the authors' experience the highest concentrations of guanidine occurred in patients presenting rapid loss of fluid in diarrhea or having extensive necrosis in burns or acute injury of the liver, or in certain types of overwhelming infection. Apparently hyperguanidinemia is a result of secondary factors rather than an essential feature of any particular disease. The intoxications seen clinically are in many respects similar to intoxication produced by experimental guanidine poisoning and are relieved by calcium therapy. The authors believe that calcium medication is a valuable supplement to the common therapeutic measures employed in the management of such toxemias.

American Journal of Medical Sciences, Philadelphia

186: 313-460 (Sept.) 1933

Acetyl-β-Methylcholin: I. Action on Normal Persons, with Note on Action of the Ethyl Ether of β-Methylcholin. I. Starr, Jr., K. A. Elsom and J. A. Reisinger, with introduction by A. N. Richards, Philadelphia.—p. 313.

Id.: II. Action on Gastro-Intestinal Tract of Normal Persons, in Abdominal Distention, and in Certain Other Conditions. W. O. Abbott, Philadelphia.—p. 323.

Id.: III. Its Action on Paroxysmal Tachycardia and Peripheral Vascular Disease, with Discussion of Its Action in Other Conditions. I. Starr, Jr., Philadelphia.—p. 330.

*Diagnostic Test for Infectious Mononucleosis. W. W. Bunnell, New Haven, Conn.—p. 346.

Instance of Lymphatic Leukemia Following Benzol Poisoning. E. H. Falconer, San Francisco.—p. 353.

Advantages of Intramuscular Injections of a Solution of Liver Extract in Treatment of Pernicious Anemia. W. P. Murphy, Boston.—p. 361.

Congenital Aorticoventricular Fistula with Engrafted Acute Suppurative Endocarditis. M. Jacobi and A. Heinrich, Brooklyn.—p. 364.

*Serial Nonprotein Nitrogen Studies and Their Prognostic Significance in Acute Coronary Occlusion: Preliminary Report. C. L. Steinberg, Rochester, N. Y.—p. 372.

Serum Calcium in Normal Boys. M. Molitch, S. Weinstein and R. F. Cousins, Jamesburg, N. J.—p. 378.

Calcium Precipitations and Alkalization in Aerobic Tissue Cultures. W. C. Hueper and Mary A. Russell, Philadelphia.—p. 383.

*Typhoid Vaccine in the Treatment of Chorea. A. Capper and E. L. Bauer, Philadelphia.—p. 390.

Spontaneous Rupture of the Esophagus: Report of Four Cases. R. Gott, Jr., Louisville, Ky.—p. 400.

Amebiasis in Northern New Jersey. M. Asher and M. Kraemer, Newark, N. J.—p. 409.

Arachnoidism: Report of a Series of Twenty-Nine Cases of Poisoning from the Bite of Latrodectus Mactans. G. Walsh and W. G. Morgan, Fairfield, Ala.—p. 413.

Diagnostic Methods and Metabolic Studies in Disease of Biliary Tract: I. Description of Routine Examination and Discussion of Normal Standards. J. R. Twiss and J. A. Killian, New York.—p. 418.

Galactose Tolerance as a Measure of Liver Function. J. H. Roe and A. S. Schwartzman, Washington, D. C.—p. 425.

Diagnostic Test for Infectious Mononucleosis.—Bunnell employed the sheep cell agglutinin test in more than 2,000 cases representing seventy-six clinical conditions. With the exception of serum disease, he has been unable to demonstrate an appreciable increase of heterophil agglutinins for sheep cells in the serums above the normal dilution of 1:8. In fifteen cases of infectious mononucleosis he observed a consistent increase in all cases. The titers, ranging from 1:64 to 1:4,096, apparently depended to a considerable extent on the stage of the disease at which the serum was obtained and on the severity of the illness. None of the common conditions manifesting a similar clinical picture, such as acute adenitis, tuberculous or syphilitic adenitis, Hodgkin's disease, acute or chronic lymphatic or myelogenous leukemia, aplastic anemia, hemorrhagic purpura, agranulocytic angina or Vincent's angina, have shown an increase in heterophil agglutinin titer. Cases presenting a suggestive clinical and blood picture, whose blood serum shows an agglutination for sheep cells in a dilution of at least 1:64, can apparently safely be diagnosed as infectious mononucleosis, and a favorable prognosis given.

Nonprotein Nitrogen and Acute Coronary Occlusion.—Steinberg emphasizes the function of the kidney in coronary occlusion. A certain pressure is needed in the arterial system

for the kidney to carry on its normal function. His observations in acute coronary occlusion do not coincide with the thought that in essential hypertension the elevated blood pressure is a safety mechanism so that the vital renal function may be performed. He presents sixteen cases, in two of which the drop in blood pressure and a definite and marked diminution in urinary output are not sufficient in themselves to account for the nonprotein nitrogen factor in acute coronary occlusion; for, although both had a decided and marked drop in blood pressure and a diminution in urinary output, the nonprotein nitrogen did not become markedly elevated. His study of the retention of nonprotein nitrogen in the blood plasma in the sixteen cases of coronary occlusion indicates that nine showed a nonprotein nitrogen retention that was above 40 mg. per hundred cubic centimeters (one had 40 mg.). Of the six fatal cases, only one showed a nonprotein nitrogen below 40, and three showed progression or retention of waste products in the blood stream or continued elevation without necessarily progression in the amount of nonprotein nitrogen. Three patients in whom serial nonprotein nitrogen studies were made and who showed a definite tendency toward lowering of the nonprotein nitrogen value recovered. None of the cases examined post mortem showed evidence of any marked nephritis.

Typhoid Vaccine in Treatment of Chorea.—Capper and Bauer treated twenty-three cases of chorea, nine of which were chronic, by means of typhoid-paratyphoid vaccine intravenously: nineteen were entirely symptom free at the time of discharge from the hospital. Of the nine chronic cases in which the average duration of the symptoms was four and one-half years, one showed a persistent talkativeness and one a persistent blinking of the eyes, but all other symptoms had disappeared. One patient who suffered from chorea for two months was improved following the vaccine injections, but the authors were unable to continue their observations because of a transfer to another hospital soon after the injections were completed. Only one of the twenty-three cases, a subchronic one, was definitely refractory, and the twitchings and irregular movements persisted in spite of the treatment; nevertheless, when the patient returned three months later for follow-up examination, he was entirely well. A reexamination of eleven cases, from three to fifteen months subsequent to discharge, showed seven and possibly eight to be entirely well, in spite of the fact that over 50 per cent of them belonged to the class of chronic chorea. No untoward effects were noticed in any of the patients from the vaccine injections. The authors' method consisted in injecting intravenously a mixture of typhoid, paratyphoid A and paratyphoid B vaccine, each cubic centimeter containing 500,000,000 of typhoid and 250,000,000 each of paratyphoid A and B organisms. The initial dose was from 0.15 to 0.2 cc. When the patient did not react to the initial dose or to an increase of 0.1 cc. daily, the increase in dosage was made more rapidly. The injections were continued daily, usually for six or seven days, when a rest period of several days was instituted. If the child did not recover completely after the first series of six or seven injections, a second, third or even fourth series of injections was instituted.

American J. Obstetrics and Gynecology, St. Louis

26: 311-470 (Sept.) 1933

Recent Advances in Study of Etiology and Treatment of Eclampsia Gravidarum. J. Hofbauer, Baltimore.—p. 311.
Induction of Labor by Means of Artificial Rupture of Membranes, Castor Oil and Quinine, and Nasal Pituitrin. D. G. Morton, San Francisco. —p. 323.
*Disturbances of Menstruation Due to Simple Achlorhydric Anemia. R. L. Haden, Cleveland, and J. M. Singleton, Kansas City, Kan. —p. 330.
Nature of Periods of Sex Desire in Woman and Their Relation to Ovulation. O. L. Tinklepaugh, Orange Park, Fla.—p. 335.
Tetanospasmodic Uterine Rings: Report of Four Cases. J. Weiss, New York.—p. 346.
Primary Carcinoma of Oviduct. J. A. McGlinn and W. B. Harer, Philadelphia.—p. 354.
Some Statistics of Postpartum Hemorrhage. C. H. Peckham and K. Kuder, Baltimore.—p. 361.
Analysis of Two Hundred Cases of Septic Abortion Treated Conservatively. J. T. Witherspoon, New Orleans.—p. 367.
*Preventing Postnatal Loss of Weight in the New-Born. I. N. Kugelmass, Ruth E. L. Berggren and Mildred Cummings, New York.—p. 375.
Rupture of Cesarean Scar in Succeeding Pregnancy. W. R. Nicholson, Philadelphia.—p. 387.
Premature Rupture of Membranes and Its Effect on Labor. L. W. Mason, Denver.—p. 394.
Application of Universal Joint to Obstetric Forceps. J. Mann, Toronto. —p. 399.
*Evaluation of Alurate (Allyl-Isopropyl-Barbituric Acid) as Premedication Agent in Surgery: Preliminary Report. M. L. Axelrod, Cleveland.—p. 404.
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Spinal Anesthesia in Series of Three Hundred Abdominal and Pelvic Operations. P. N. Charbonnet, Tulsa, Okla.—p. 412.
An Analysis of Two Hundred Cases of Spinal Anesthesia. M. Sabel, Philadelphia.—p. 417.
Cervical Cauterization Under Parametrial Anesthesia. L. Braun, Detroit. —p. 421.
Dührssen's Incisions of the Cervix. M. M. Shir, Brooklyn.—p. 425.
Granulosa Cell Tumors of the Ovary: Report of Two Cases. S. A. Wolfe and S. Kaminester, Brooklyn.—p. 434.
Toxic Neuronitis of Pregnancy. S. Lubin, Brooklyn.—p. 442.
*Technic of Injection of Pudendal Nerve and Branches of Small Sciatic Nerve with Observations Made on One Hundred Cases of Delivery. Elizabeth O'Hearn and C. H. Kramer, Mahanoy City, Pa.—p. 444.
Intravenous Pituitary Extract in Low Cervical Cesarean Section: Report of One Hundred Cases. R. J. Heffernan, Boston.—p. 446.
Hydrops Tubae Profluens Complicating Chronically Perforating Appendicitis: Report of a Case in a Girl of Twelve Years. A. T. Walker, Mare Island, Calif.—p. 448.
Dystocia Due to Carcinoma of the Rectum and of the Vagina. W. F. Mengert, Philadelphia.—p. 451.
Rupture of Symphysis Pubis During Labor: Case. P. A. D'Acierno, Union City, N. J.—p. 453.
Sarcoma of Uterus Complicating Pregnancy. M. G. DerBrucke, Brooklyn.—p. 457.
Extraneous Foreign Bodies in the Urinary Bladder, with Especial Reference to Their Occurrence Among Women. L. C. Scheffey and C. Lintgen, Philadelphia.—p. 460.
Acute Intestinal Obstruction Complicating Labor. E. M. Lazard, Los Angeles.—p. 462.
Wandering Fibroid in Rectovaginal Septum. J. P. Long, Jr., Memphis, Tenn.—p. 463.
Placenta Praevia with Twins. C. D. McCann, Brockton, Mass.—p. 464.

Menstrual Disturbances Due to Achlorhydric Anemia.—Haden and Singleton studied the menstrual disturbances in twenty-nine cases of simple achlorhydric anemia. Abnormalities of menstruation are found commonly in this disease and constitute one of its most characteristic features. Achlorhydria with idiopathic hypochromic anemia is pathognomonic of the disease. The disease probably belongs in the deficiency group and responds well to the administration of adequate doses of iron. Simple achlorhydric anemia should be suspected in all cases of unexplained menstrual disturbances and the suspicion verified or excluded by gastric analysis and careful blood examination. In the authors' series the menstrual disturbances occurred almost as frequently as symptoms due directly to the low hemoglobin content of the blood.

Loss of Weight in the New-Born.—Kugelmass and his associates point out that the initial loss in weight in the newborn can be prevented by the oral administration of a solution consisting of 6 per cent gelatin (p_H 6.2), 3 per cent dextrose and 0.5 per cent sodium chloride at intervals of two hours throughout the twenty-four-hour cycle immediately after birth. The characteristic clinical picture of the new-born is a result of birth shock and is more effectively combated by a hydrating solution than by milk mixtures during the first two or three days of life. The total fluid intake of the new-born properly conditioned to both the breast and the bottle was as much as twice that of the series receiving the routine nursery care. Preventing the loss of weight in the new-born produces rapid disappearance of the so-called physiologic apathy, somnolence and stupor secondary to birth shock and the compensated acidosis universally present. The new-born infant shows a hypoglycemia during the first days of life and a sugar tolerance curve of low peak, thus indicating a dire need for carbohydrate as well as a tendency to utilize, store and exhaust their endogenous supply of carbohydrate more rapidly than older children. Determinations of the refractive index and viscosity of the serum of the new-born revealed the concentration of the blood on the first days of life, gradually attaining normal values following administration of food in the control series; but the new-born treated with the hydrating solution showed a markedly constant course for both refractive and viscosimetric curves. The gelatin component of the hydrating solution decreased the clotting time to less than three minutes, in comparison with seven minutes in the control series.

Premedication Agent in Surgery.—Axelrod studied the advantages of allyl-isopropyl-barbituric acid (alurate) in 150 surgical cases. He found the barbiturate to have definite clini-

cal advantages as previously suggested by animal experimentation. The oral administration of the substance, in tablet or capsule form, is a satisfactory method. The optimal dose appears to be 10 mg. per kilogram of body weight (i. e., approximately 1 grain [0.065 Gm.] for every 15 pounds of body weight, excessive fat, as in obese patients, being discounted). Using a divided dosage is rational and satisfactory. Side actions occur less often than have been reported from large single doses of other barbiturates. The volume of the anesthetic can be appreciably reduced. There does not seem to be any marked delay in the occurrence of the postoperative reaction. The need for postoperative nursing care not only is not increased, as reported for some barbiturates, but is diminished in most cases.

Injection of Pudendal Nerve.—O'Hearn and Knauer used the following technic in seventy-six private and twenty-four ward patients: With the patient in the gynecologic position the inner margin of the tuberosity of the ischium is located and, at a point on a line with the anus but close to the ischium, the tip of the needle is inserted in the direction of the spine of the ischium, which is palpated through the vagina or rectum. The tip of the needle when inserted about 5 cm. encounters the resistance of the perineal fascia, beyond which there seems to be an open cavity. The pudendal nerve leaves the pelvis through the greater sacrosciatic foramen, circles the spine of the ischium and reenters the pelvis through the lesser foramen. Therefore, by palpating the spine with the fingers of one hand and using it as a guide, it is possible to inject the solution at the proximal edge of the spine and cause complete anesthetization of the pudendal nerve and the structures which it supplies. Ten cc. of a 1:500 solution of pantocain is injected into this region. The needle is withdrawn until its tip is free from the perineal fascia and then is redirected upward and outward onto the face of the tuberosity of the ischium, when the remaining 3 to 5 cc. of the solution is injected. This solution is massaged upward over the surface of the tuberosity, through the potential space existing between the gluteus maximus muscle and the tendinous insertions of the extensor group of muscles, thereby anesthetizing the perineal branches of the small sciatic nerve, which are constantly present in this space. A complete anesthesia to the sense of pain was manifested in all the structures composing the floor of the perineum, including the lower third of the vagina and the posterior half of the labia majora, and the perineum may be "ironed out" painlessly as well as sutured. The time of injection is not until the head is on the perineum and the membranes are ruptured and every assurance is offered that the continuance of labor will not exceed four and a half hours, which is the average duration of this anesthetic with 1 cc. of 1:1,000 epinephrine added. Its effect, without epinephrine, continues for two hours.

American Journal of Physiology, Baltimore

105: 497-726 (Sept. 1) 1933. Partial Index

Differences Between Anterior Pituitary Sex-Stimulating Hormones and Pregnancy-Urine Substances as Tested in the Male Mammal and Bird. J. A. Schockaert, New York.—p. 497.
Action of Thyroxine on Tissue Respiration. J. A. Dye, Ithaca, N. Y. —p. 518.
The Sherrington Phenomenon: V. Nervous Pathways. J. C. Hinsey and C. C. Cutting, San Francisco.—p. 535.
Studies in Normal Human White Blood Cell Picture: I. Variations in Recumbent Basal Subjects and in Individuals with Change of Posture. E. Jones, D. J. Stephens, Harriett Todd and J. S. Lawrence, Rochester, N.Y.—p. 547.
Studies on Thyroglobulin: III. Thyroglobulin Content of Thyroid Gland. B. O. Barnes and Mildred Jones, Chicago.—p. 556.
Pulmonary Artery Pressures. C. F. Horine and C. G. Warner, Baltimore.—p. 562.
Effect of Diet on Response to Parathyroid Extract and Vitamin D: III. Effect of Low Calcium-High Phosphorus Diets in Dogs. Agnes Fay Morgan, E. Alta Garrison and Marguerite J. Hills, Berkeley, Calif.—p. 608.
*Variations of Intragastric Temperature in Response to Vasodilating Agents. N. W. Thiessen and A. M. Snell, Rochester, Minn.—p. 665.
Sugar in Blood and Subcutaneous Lymph Following Insulin Administration. J. W. Heim, Boston, and B. N. Berg, New York.—p. 674.
Further Quantitative Studies in Absorption: Influence of Acetylcholine on Absorption of Glucose. E. Gellhorn and D. Northup, Chicago.—p. 684.
Proteins as Stimulants for the Secretion of Pepsin. Elizabeth R. B. Smith and G. R. Cowgill, New Haven, Conn.—p. 697.

Variations of Intragastric Temperature.—Thiessen and Snell studied the variations of intragastric temperatures of patients suffering from ulcers of the gastro-intestinal tract in relation to vasodilating drugs and test meals. After stimulation with histamine, the mean rise in oral temperature was 0.25 C., and the mean rise in rectal temperature was 0.19 C. The mean fall in intragastric temperature was 0.18 C. initially, and then it made a rise above the initial temperature comparable to the rise noted in rectal and oral readings. After acetylcholine, the intragastric temperature rose on an average 0.16 C., as compared to a rise of 0.08 C. for the rectal temperatures and insignificant variations in oral temperatures; it made a sharp rise at the two hour reading. A peripheral and visceral dissociation was not so marked after the administration of acetylcholine as when histamine was used. After the administration of alcohol, the rectal and oral temperatures rose gradually. After an initial drop, the mean rise of intragastric temperature was 0.4 C.; then the temperature dropped to normal. A definite splanchnoperipheral dissociation was apparent in 60 per cent of the experiments. The dissociation of visceral from peripheral reactions affecting the temperature was most apparent after the administration of histamine, less so but fairly definite after alcohol, and variable after acetylcholine. In the presence of artificially produced fever the maximal mean rise of oral temperature was 0.56 C., of the rectal temperature 0.59 C., and of the intragastric temperature 1 C. In only 20 per cent of the cases was a definite splanchnoperipheral dissociation seen, although this phenomenon may have been overlooked in the other 80 per cent. The theoretical relationship of splanchnic vasodilatation to temperature has been considered. Additional evidence has been presented to support the concept of a splanchnoperipheral balance.

American Review of Tuberculosis, New York

28: 293-410 (Sept.) 1933

*Shrunken Pulmonary Lobe with Chronic Bronchiectasis. O. R. Jones and A. Cournand, New York.—p. 293.
Heart and Tuberculosis: Mediastinal Distortion as a Source of Circulatory Embarrassment. D. M. Brumfiel, Saranac Lake, N. Y.—p. 317.
Experimental Bone and Joint Tuberculosis in Rabbits. P. J. Trudel, Perrysburg, N. Y.—p. 331.
Investigation and Operative Exploration and Treatment of Old Tuberculous Cavitation, with Especial Reference to Pneumonocavernolysis. H. Neuhof, Secaucus, N. J.—p. 344.
Secondary Diaphragmatic Rises Following Phrenic Neurectomy. D. O. N. Lindberg, Decatur, Ill.—p. 352.
Tuberculous Lung in Which a Large Emphysematous Bulla Was Mistaken for a Cavity. W. S. Miller, Madison, Wis.—p. 359.
Tuberculosis in the Hawaiian: Study of School Children of Hawaiian Blood. F. J. Halford, Honolulu, Hawaii.—p. 370.
Tuberculosis in Infants and Primitive Races. Wathena Myers Johnson and J. A. Myers, Minneapolis.—p. 381.

Shrunken Lobe with Bronchiectasis.—Jones and Cournand present, as an entity, the shrunken pulmonary lobe with chronic bronchiectasis and prove by clinical observations two probable mechanisms in the causation of pulmonary shrinkage: bronchial stenosis and chronic inflammation of the lung. In many instances a combination of these two pathologic states exists, as shown by one of their cases. They believe that, besides the stenosis of a bronchus from outside pressure due to congested lymph nodes, the loss of the normal bronchial function and the inflammation of the bronchial tree by infection from the lymph nodes are definite factors in the causation of bronchiectasis. The authors are fully aware of the fact that there are many other causes of bronchial stenosis with resultant pulmonary shrinkage, but they do not discuss them, as the cases they present seem to them to be attributable to bronchial stenosis and chronic inflammation of the lung. They discuss the question of the congenital origin of this condition and present two cases of chronic bronchiectasis with shrunken lobes due to possible congenital causes.

Archives of Internal Medicine, Chicago

52: 341-496 (Sept.) 1933

Ultimate Results of Thoracoplastic Operations in Pulmonary Tuberculosis. J. J. Wiener and M. Fishberg, New York.—p. 341.
*Iron in Human Blood. A. Sachs, V. E. Levine and A. Appelsis, Omaha. —p. 366.
Insensible Perspiration: Its Relation to Basal Metabolism. G. E. Wilson, Seattle.—p. 378.
*Therapeutic Application of Acidophilus Milk in Simple Constipation: Report of Thirty-Six Cases. L. Weinstein, J. E. Weiss, L. F. Rettger, New Haven, Conn., and M. N. Levy, Bridgeport, Conn.—p. 384.

Cinchophen Poisoning: Report of Two Cases with Histologic Observations. H. H. Pernar and H. D. Goehring, Pittsburgh.—p. 398.
Fatty Infiltration of the Myocardium. O. Saphir and M. Corrigan, Chicago.—p. 410.
Cardiac Weights. V. Levine and J. G. Carr, Chicago.—p. 429.
Clinical Studies of Respiration: III. Influence on Expiratory Position of the Chest in Man of an Inspired Air Which Is Low in Oxygen and High in Carbon Dioxide, and of Resistance to Inspiration and to Expiration. J. A. Greene, Iowa City.—p. 447.
Id.: IV. Some Observations on Cheyne-Stokes Respiration. J. A. Greene, Iowa City.—p. 454.
*Effect on Idiopathic Hypochromic Anemia of Beef Steak (Hamburger Steak) Digested with Normal Gastric Juice. R. T. Beebe, Albany, N. Y., and M. M. Wintrobe, Baltimore.—p. 464.
Cinchophen Toxicosis: Results of Experimental Subacute and Chronic Cinchophen Poisoning. A. J. Lehman and P. J. Hanzlik, San Francisco.—p. 471.

Iron in Blood.—Sachs and his associates determined the iron content of whole blood in a large series of normal male and female subjects. They experimented on 100 medical students (men), varying in age from 20 to 25 years, and fifty nurses (women), varying in age from 20 to 30 years. They found that the average iron content of whole blood of the 100 normal men was 50.01 ± 2.56 mg. per hundred cubic centimeters. The average for the fifty normal women was 42.67 ± 2.13 mg. per hundred cubic centimeters. The blood of women has a definitely lower iron content than that of men. Iron in whole blood is almost entirely linked with the hemoglobin molecule. Since the quantity of nonhemoglobinous iron present in the serum and the cellular elements is very small, the error in calculating hemoglobin from whole blood iron is negligible. On the basis that hemoglobin contains 0.335 per cent of iron, the authors conclude that the average normal blood of men contains 14.93 ± 0.76 Gm. of hemoglobin per hundred cubic centimeters, while the average normal blood of women contains 12.74 ± 0.66 Gm. per hundred cubic centimeters. By dividing the number of milligrams of iron per hundred cubic centimeters of blood by the first three figures of the red blood cell count, a quotient, which Murphy, Lynch and Howard designated as the iron index, is obtained. The authors found the iron index for normal men to be 10.01 ± 0.65 Gm., and for normal women 9.6 ± 0.56 Gm. of hemoglobin per hundred cubic centimeters. The iron index is preferable to the color index because of the greater accuracy with which the former may be determined. The iron color index, based on the ratio of the percentage of iron to the percentage of red blood cells, is also preferable to the older hemoglobin color index. The advantages to be derived from the clinical use of this index lie in its accuracy and in the retention of the convenient + 1 or — 1 designation of the older hemoglobin color index.

Acidophilus Milk in Constipation.—Weinstein and his associates treated thirty-six patients suffering from simple chronic constipation with acidophilus milk (1 quart daily), the cultures of which were known to be of high viability. All were ambulant. Of the patients who underwent the treatment, twenty-seven reacted favorably and seven responded negatively, and in their cases the treatment was regarded as having failed. Two gave results that were neither positive nor negative. Of those who responded positively, fourteen were so-called implanters; that is, they maintained a high acidophilus content in the intestine for from twelve to sixteen weeks after the discontinuance of the last course of milk treatment. During this period, no return to the former condition of constipation was noted. Two other patients showed distinct improvement sixteen weeks after the cessation of the treatment but Bacillus acidophilus was not demonstrable in their feces. The results indicate that the most favorable response will be obtained by the continued use of the milk over reasonably long periods, with interruptions (so-called rest periods) of from four to twelve weeks or even longer. Whether the administered aciduric organism actually becomes implanted in the intestine of the patient who responds positively after many weeks of feeding and intermission, or whether the constant application of the acidophilus milk under favorable conditions of diet (with milk, lactose or dextrin) stimulates to activity similar or closely related strains native in the intestine must be left an open question. Either of these two eventualities should lend strong support to the acidophilus principle.

Idiopathic Hypochromic Anemia.—Beebe and Wintrobe gave five patients suffering from idiopathic hypochromic anemia beef steak with normal gastric juice, according to the method used by Castle in causing a remission in pernicious anemia. In no instance was there an increase in the percentage of reticulocytes or a rise of the hemoglobin, the volume of packed red cells or the red blood count. Following the administration in each instance of suitable amounts of iron ammonium citrate, the percentage of the reticulocytes rose promptly and there soon followed a rapid increase of hemoglobin, an increase in the volume of packed red blood cells and improvement in the patients' symptoms and general appearance.

Delaware State Medical Journal, Wilmington

5: 195-222 (Sept.) 1933

Recent Advances in Treatment with Historical Notes. H. I. Goldstein, Camden, N. J.—p. 195.
Value of Diet in Treatment of Arthritis and Migraine. M. B. Holzman, Wilmington.—p. 212.

Florida Medical Association Journal, Jacksonville

20: 89-138 (Sept.) 1933

Review of Some Urinary Anomalies and Pathologic Conditions Producing Symptoms of Especial Interest to the General Practitioner. R. J. Holmes and M. M. Coplan, Miami.—p. 99.
Carcinoma of the Colon: Plea for Recognition of Early Symptoms. G. M. Dawson, West Palm Beach.—p. 106.
Cesarean Section: Phase in the Unwise Modern Obstetric Trend. R. W. Holmes, Chicago.—p. 110.

Georgia Medical Association Journal, Atlanta

22: 319-360 (Sept.) 1933

Diagnosis and Treatment of Aneurysm. J. L. Campbell, Atlanta.—p. 319.
Bismuth Poisoning in Treatment of Syphilis. J. W. Brittingham, Augusta.—p. 323.
Operative Technic and Postoperative Treatment of Fulminating Appendicitis. J. T. McCall, Rome.—p. 327.
Management of Chronic Arthritis. G. J. Dillard, Columbus.—p. 332.
Prevention of Deafness. J. A. Smith, Macon.—p. 338.
Diagnosis and Treatment of Bronchiectasis with Iodized Oil. W. G. Elliott, Cuthbert.—p. 340.
Rupture of Uterus During Labor. R. Bell, Thomasville.—p. 342.
Oral Treatment of Syphilis in Negro Children with Acetarsone (Stovarsal). J. Yampolsky, laboratory collaboration by D. F. Cathcart and I. Smith, Atlanta.—p. 344.
Use of Salyrgan in Cardiac Decompensation with Edema: Case Report. R. W. Dickson, Atlanta.—p. 348.

Illinois Medical Journal, Chicago

64: 209-304 (Sept.) 1933

The Diagnosis of Chronic Arthritis. D. Boyd, Highland Park.—p. 229.
Treatment of Arthritis by Electropyrexia. D. E. Markson and S. L. Osborne, Chicago.—p. 231.
Methods of Producing Hyperpyrexia by Various Physical Agents. J. R. Merriman and S. L. Osborne, Chicago.—p. 237.
*Endocrine Dyscrasias and Mental Disorders: Preliminary Report. J. H. Hutton, Chicago; R. Brandon, Springfield; C. F. Read and J. T. Nerancy, Elgin.—p. 242.
Foreign Bodies in the Esophagus. C. U. Collins, Peoria.—p. 247.
Id. C. D. Sneller, Peoria.—p. 250.
Relation of the Health Officer to the Community. A. Ailes, La Salle.—p. 253.
Etiology of Ocular Disease. H. S. Gradle, Chicago.—p. 258.
Care of the Indigent. R. K. Packard, Chicago.—p. 261.
Military Hygiene. J. P. Hitchens, Fort Sheridan.—p. 264.
Physical Measures in Hypertrophic Rhinitis. A. R. Hollender, Chicago.—p. 269.
Value of Combined Cholecystographic and Liver Function Studies. H. Swanberg, Quincy.—p. 273.
Perineal Lacerations: Method of Conducting the Second Stage of Labor Which Will Lessen Their Occurrence. R. F. Weisbrenner, Chicago.—p. 274.
Surgery of Thyroid in Children. W. L. Bowen, Peoria.—p. 277.
The Master in the House of Medicine. A. M. Schwitalla, St. Louis.—p. 280.
What I Would Tell a Lay Audience About Venereal Diseases. Carolyn N. Macdonald, Chicago.—p. 2a8.
Some of the Obstetric Problems of the Country Doctor. E. E. Davis, Avon.—p. 294.
Socialization of Medicine. E. F. Garraghan, Chicago.—p. 298.

Endocrine Dyscrasias and Mental Disorders.—Hutton and his associates attempted to determine whether there was a relationship between endocrine dyscrasias and mental disorders and whether correction of the endocrine disturbance would be valuable in the treatment of mental disorders. The pituitary products used were a commercial soluble extract from the anterior lobe of the pituitary (antuitrin) and posterior lobe extracts. They were administered hypodermically three times

a week in such doses as the patient could tolerate. The dose of posterior lobe extracts was kept below that which produced unpleasant abdominal cramps. The anterior lobe extract was given in doses of from 0.5 to 1 cc., depending on the patient's tolerance. Ovarian medication consisted of the residue or of one of the standardized preparations, more often the residue, and one ampule was given subcutaneously three times a week. If a standardized preparation was used, it was given on alternate days beginning a week before the expected menstrual period. Thyroid has been given by mouth. Of 172 patients recognized as having some endocrine defect, 26.7 per cent are now paroled or discharged, whereas the discharged and paroled patients from all the state institutions during the year ended June 1931 were only 17.3 per cent. This does not mean that endocrine therapy will replace the accepted psychiatric routine but that endocrine therapy should become a routine adjuvant to the psychiatric procedure when indicated.

Journal of Allergy, St. Louis

4: 455-570 (Sept.) 1933

Allergen Content of Pollen Extracts: Its Determination and Its Deterioration. A. Stull, R. A. Cooke and Jean Tennant, New York.—p. 455.
Use of Glycerolated Pollen Extracts in Treatment of Hay Fever. A. Brown, New York.—p. 468.
Further Observations on Changes in Skin Tests Following Specific Pollen Therapy. A. Colmes and F. M. Rackemann, Boston.—p. 473.
Status Asthmaticus or Severe Subacute Asthma. J. A. Clarke, Jr., Philadelphia.—p. 481.
Allergy a Constant Factor in Etiology of So-Called Mucous Nasal Polyps. R. A. Kern and H. P. Schenck, Philadelphia.—p. 485.
Further Observations on Nature of Allergy. F. M. Rackemann, F. A. Simon, Margaret G. Simon and Margaret A. Scully, Boston.—p. 498.
*Hypersensitiveness to Acetylsalicylic Acid Expressed by an Angina Pectoris Syndrome With and Without Urticaria. C. Shookhoff and D. L. Lieberman, Brooklyn.—p. 506.
Angina Pectoris Syndrome, Activated by Ragweed Sensitivity in a Patient with Coronary Vessel Sclerosis: Case Report. C. Shookhoff and D. L. Lieberman, Brooklyn.—p. 513.
*Treatment and Prevention of Rhus Toxicodendron Poisoning. G. H. Gowen, Chicago.—p. 519.
Common Wood Tansy (Tenacetum Vulgare) as a Cause of Eczematous Dermatitis. C. A. Greenhouse and Marion B. Sulzberger, New York.—p. 523.
Contact Dermatitis Due to a Common Plant. C. H. Harville, Warsaw, N. Y.—p. 527.
Extreme Hypersensitiveness to Heat: Report of Case. O. Swineford, Jr., and H. Weinberg, University, Va.—p. 530.
*Urinary Proteose in Allergic Conditions. L. Tuft and M. Brodsky, Philadelphia.—p. 534.
Treatment of Bronchial Asthma by Sterile Abscess Formation. W. Lintz, Brooklyn.—p. 540.

Hypersensitivity to Acetylsalicylic Acid.—Shookhoff and Lieberman report three cases of hypersensitivity to acetylsalicylic acid expressed by a syndrome of angina pectoris, accompanied in two cases by urticaria. None of the characteristic signs of myomalacia of the heart were present. A study of one case showed definite allergic manifestations and definite electrocardiographic changes in the attack produced by the ingestion of acetylsalicylic acid. The electrocardiographic changes disappeared before the subsidence of the reaction. This syndrome was produced in the patient with every administration of acetylsalicylic acid and was to some degree controlled by the administration of epinephrine. There were evidences of preexisting cardiovascular disease in all three patients.

Rhus Toxicodendron Poisoning.—Gowen used the almond oil extract of Rhus toxicodendron in the treatment and prevention of eight cases of Rhus toxicodendron poisoning. The patients were from 5 to 54 years of age. One injection in the spring will protect susceptible persons for approximately one year. Injection of the almond oil extract not only is satisfactory therapeutically but also offers protection for the rest of the season and leads to milder attacks the ensuing year. Two patients were immune for one year without treatment after several annual injections. In two patients who are exposed annually, immunity has been present for two years in one and five years in the other. The site of injection was the deltoid in adults and older children and the gluteal muscles in the young children. The skin was sterilized with tincture of sodium of ethylmercurithiosalicylate, the injection was made deep into the muscle, and a large drop of collodion was placed round the site of injection before the needle was withdrawn. This prevented any egress of Rhus toxin and eliminated the possibility of any local dermatitis of the skin round this area. In no case was less than 1 cc. (one injection) of extract used. More than two injections were never needed. Noticeable improvement varied from one to three days after injection.

Urinary Proteose.—Tuft and Brodsky demonstrated the presence of an ether-extractable substance, described as "urinary proteose" by Oriel, in the sixty-one examinations of the urine of forty-two allergic patients in slightly larger amounts than in the nonallergic controls, and, although larger amounts were eliminated than in the quiescent periods, positive skin reactions of a specific character could not be elicited nor was treatment in three cases of chronic asthma followed by any improvement. It is doubtful from these observations and a review of the literature whether the proteose of Oriel has a specific immunologic basis.

Journal of Lab. and Clinical Medicine, St. Louis

18: 1203-1318 (Sept.) 1933

Insulin Resistance and Sensitivity. W. G. Karr, C. W. Scull and O. H. Petty, Philadelphia.—p. 1203.
*Glucose Tolerance Curves in Pulmonary Tuberculosis: Observations on One Hundred Cases. D. W. Kramer, with technical assistance of Freda Ward, Philadelphia.—p. 1212.
Cholelithiasis: Statistical Study, with Especial Reference to Its Frequency in the Colored Race. R. H. Jaffe, Chicago.—p. 1220.
Study of Total and Ultrafiltrable Calcium and Acid-Soluble Phosphate Content of Blood Serum of Four Hundred and Twenty-Two Healthy Children. Marion Smoot Needels and C. M. Marberg, Chicago.—p. 1227.
Study of Dimethylaminobenzaldehyde Test for Atropine. Arlie A. O'Kelly and C. F. Poe, Boulder, Colo.—p. 1235.
Significance of Membranes in Mucous Form of Colitis. J. Friedenwald and S. Morrison, Baltimore.—p. 1242.
Some Factors Responsible for So-Called Self-Disinfecting Power of the Skin. C. S. Bryan and W. L. Mallmann, Lansing, Mich.—p. 1249.
*Possibility of Pressor Principle in Blood of Persons with Hypertension: Experimental Study. A. H. Elliot and F. R. Nuzum, Santa Barbara, Calif.—p. 1255.
Monocytic Leukemia. W. M. Fowler, Iowa City.—p. 1260.
Simple One-Stage Technic for Hepatectomy in the Dog: Some Remarks on Clinical Symptomatology of Terminal Hepatic Insufficiency. J. Markowitz, W. M. Yater and W. H. Burrows, Washington, D. C.—p. 1271.
*Determination of Nonprotein Nitrogen, with Especial Reference to Koch-McMeekin Method. C. A. Daly, Albany, N. Y.—p. 1279.
Micro-Kjeldahl Still. T. P. Nash, Jr., Memphis, Tenn.—p. 1285.
Study of Kolmer, Kahn and Kline Tests with Spinal Fluids. Lucy S. Heathman and Margaret Higginbotham, Minneapolis.—p. 1287.

Pulmonary Tuberculosis.—Kramer studied the curves of the blood sugar of 100 tuberculous patients divided in two series, series A including patients who at one time or other had glycosuria and series B being the control group. The fasting blood sugars were invariably of normal range. Diabetic patients were not included. The author offers suggestions for classifying the curves of the blood sugar: type I, the high or diabetic curve; type II, the normal curve, and type III, the low curve. There were seventeen patients showing a high or diabetic curve. Twelve of this number were found in series A. Eighty-three patients had nondiabetic curves; fifty-nine were normal and twenty-four showed low curves. The 17 per cent diabetic curves were much below the figures mentioned by some authors. The influence of the state of the tuberculosis on the curve of the blood sugar is indefinite. Although an occasional case of increased tolerance for carbohydrates may be observed in the late stages of tuberculosis, the author was unable to point out any direct bearing on the curves in the patients studied. He believes that the low proportion of diabetic curves and the comparatively high percentage of low curves may be interpreted as an indication that tuberculous patients have a higher tolerance for sugar and may explain the rarity of diabetes developing in tuberculosis.

The Pressor Principle, the Blood and Hypertension.—With a mercury manometer, Elliot and Nuzum registered the carotid blood pressure of a full grown rabbit under anesthesia with sodium amytal (0.08 Gm. per kilogram of body weight in the vein of the ear). The blood to be tested was drawn with a large needle from the antecubital vein and the syringe emptied into a flask containing enough sodium citrate to make a total concentration of 0.4 per cent. The blood was brought immediately to the laboratory and injected into the external jugular vein of the rabbit. The lapse of time from the with-

drawal of the blood to its injection was about five minutes. The amount of blood injected was 3 cc. per kilogram of body weight. The lethal dose of the blood from persons both with normal blood pressure and with hypertension was approximately the same (from 6 to 8 cc. per kilogram). The patients from whom the blood was obtained were carefully studied as to renal function, degree of arterial disease and height and lability of the blood pressure. With the exception of one patient who had malignant hypertension and renal failure and one who had a coronary thrombosis resulting in a lasting fall of the blood pressure, they belonged to the essential hypertensive group with constantly elevated quite stable blood pressures. Blood from laboratory workers and medical students having normal blood pressures was used for the control determinations. In most instances the result was a transitory rise of pressure followed by a prolonged fall. The average initial rise of pressure of the animals receiving blood from patients having hypertension was slightly greater and generally more prolonged than that observed in the control series. Alcohol, water and ether-soluble fractions of such blood gave uniformly a transitory fall in blood pressure. The hypothesis of a pressor principle in the blood stream of persons having consistently elevated blood pressures should be subjected to further experimental study for confirmation or refutation.

Determination of Nonprotein Nitrogen.—Daly describes a modified Koch method for the determination of nonprotein nitrogen, in which to 5 cc. of blood filtrate in a tube, graduated at 35 and 50 cc., 1 cc. of the sulphuric acid-dioxide digestion mixture 2 (prepared by adding 3 cc. of a 30 per cent solution of hydrogen dioxide to 47 cc. of the stock solution of sulphuric acid [stock solution of sulphuric acid is prepared by adding 225 cc. of concentrated sulphuric acid to 245 cc. of distilled water in a liter flask]) and two glass beads or a quartz pebble is added. This is heated with the full flame of the micro burner until the dense white fumes of sulphur trioxide appear, the mouth of the tube is closed with a small funnel and the flame is regulated until the digestion mixture barely boils. The material should be completely oxidized and the digestion mixture will be colorless. If there is a definite brown color due to unoxidized material, the digestion mixture is too weak and more dioxide should be added. The gentle heating should be continued for about two minutes and then the tube should be removed from the flame. There are usually significant amounts of dioxide present at the end of the digestion but they do not interfere when the solution is nesslerized. When occasional determinations are made it is more convenient to use digestion mixture 1 (prepared by adding 6 cc. of water to 94 cc. of the stock solution of sulphuric acid) and adding the oxidizing agent separately. When the digested material is cold, 1 cc. of a 1 per cent solution of gum ghatti is added and diluted to 35 cc. In another tube 1 cc. of digestion mixture 1 without dioxide, 3 cc. of the standard nitrogen solution and 1 cc. of solution of gum ghatti is added and diluted to 35 cc. Nessler's solution with sodium citrate, 15 cc., is measured into a small cylinder and with the 35 cc. solutions of nitrogen it is poured simultaneously into a 400 cc. beaker, whirled and poured back into the graduated combustion tube. The solutions should be at room temperature when nesslerized. After the air bubbles have disappeared the nesslerized solutions should be crystal clear. The standard and unknown solutions are nesslerized as near together as possible and read at once in the colorimeter. Calculation of the results is made in the regular way.

Maine Medical Journal, Portland

24: 161-182 (Sept.) 1933

The Challenge of Cancer. C. C. Little, Bar Harbor.—p. 165.
Preputial Cancer. F. E. Clow, Wolfeboro, N. H.—p. 169.

Medical Annals of District of Columbia, Washington

2: 197-218 (Sept.) 1933

Early Diagnosis of Cancer of Rectum and Rectosigmoid. J. Horgan, Washington.—p. 197.
Recurrent Malignant Obstruction of Prostate, Unrelieved by Prostatectomy, Treated by Transurethral Resection: Report of Five Cases. W. C. Stirling and G. A. Hopkins, Washington.—p. 200.
Results of Treatment of Gonorrheal Ophthalmia. E. J. Cummings, Washington.—p. 203.
"Apparently in Good Health Prior to the Accident." K. Garve, Los Angeles.—p. 205.

Missouri State Medical Assn. Journal, St. Louis

30: 351-388 (Sept.) 1933

Rôle of Hepatic Insufficiency in Surgical Problems. W. H. Cole, St. Louis.—p. 351.
Management of Hepatic Disease. C. A. Elliott, Chicago.—p. 356.
Relationship of the Liver to Other Visceral Organs in Disease. F. C. Helwig, Kansas City.—p. 359.
Cirrhosis of the Liver. G. H. Hoxie, Kansas City.—p. 363.
Jaundice. D. R. Black, Kansas City.—p. 366.
*Acute Abdominal Symptoms in Heart Disease. A. M. Ginsberg, Kansas City.—p. 370.
Narcolepsy. E. T. Gibson, Kansas City.—p. 373.
The Increasing Significance of Allergy in General Practice. C. J. Reis, St. Louis.—p. 376.

Abdominal Symptoms in Heart Disease.—Ginsberg states that chronic abdominal symptoms are produced by valvular disease with decompensation and disease of the coronary artery with or without decompensation. Acute abdominal symptoms are produced by (1) disease of the coronary artery (angina pectoris and coronary thrombosis), (2) valvular disease (subacute bacterial endocarditis with or without emboli, mitral stenosis and congestive heart failure, right ventricle), (3) pericardial disease (acute pericarditis with or without effusion) and (4) arrythmias (auricular fibrillation with or without emboli, auricular flutter, paroxysmal tachycardia and bundle-branch block).

New York State Journal of Medicine, New York

33: 1025-1082 (Sept. 1) 1933

Medical Aspect of Diseases of Bones and Joints. T. Howard, Brooklyn.—p. 1025.
Diagnosis of Diseases of Bones and Joints: Few Remarks Concerning the Diagnosis of Fractures. F. S. Child, Port Jefferson.—p. 1027.
First Aid in the Treatment of Fractures. O. C. Hudson, Hempstead.—p. 1029.
Common Diseases of Bones and Joints in Children. W. C. A. Steffen, Flushing.—p. 1031.
Diseases of Bones and Joints: Procedures in Physical Therapy. J. Weiss, Brooklyn.—p. 1034.
Treatment of Chronic Multiple Arthritis. G. E. Anderson, Brooklyn.—p. 1036.
Polycythemia Vera: Report of Ten Cases Treated with Phenylhydrazine. K. R. McAlpin and Katharine S. Edsall, New York.—p. 1039.
Psychopathic Personality. J. L. McCartney, Elmira.—p. 1045.
Physical Therapy in Dermatology. P. E. Bechet, New York.—p. 1049.

Ohio State Medical Journal, Columbus

29: 529-600 (Sept. 1) 1933

Littré's Hernia: A Meckel's Diverticulum in a Hernia Sac with Report of a Case. S. C. Lind, Cleveland.—p. 549.
Gas Gangrene Septicemia as Complication of Pregnancy. C. W. Pavey and H. L. Reinhart, Columbus.—p. 551.
Intravenous Liver Extract Therapy in Pernicious Anemia. W. Payne and H. H. Brittingham, Cleveland.—p. 553.
*Oral Bismuth in Treatment of Syphilis. R. O. Brigham, Toledo.—p. 556.

Oral Bismuth in Treatment of Syphilis.—Brigham treated a number of patients suffering from syphilis with glycerite of bismuth, administered orally. There has been marked improvement both clinically and serologically. The dosage is often run up to 20 minims (1.3 cc.) three times a day. In weak and poorly nourished patients this dosage shows slightly toxic results, manifested first in a soreness of the gums similar to that due to mercury. When the dosage is reduced, these symptoms quickly disappear. Glycerite of bismuth has long been used as a tonic, and patients usually remark that they feel much better after taking the bismuth preparation. In no case in which it has been used has the preparation failed to produce good clinical results, and only in a few cases did it fail to produce excellent serologic results. The medication of this form of bismuth was frequently continued for a period of three months with a brief rest and then another period of three months to clear up old cases. The oral administration of bismuth has proved a palatable way of giving the drug and is well tolerated by the patients, and many of them prefer it to hypodermic medication. The advantage over the hypodermic medication is that the patient is getting a continuous daily supply of bismuth, and not in large doses at frequent intervals.

West Virginia Medical Journal, Charleston

29: 363-400 (Sept.) 1933

Infant Mortality: Sensitive Index of Social Welfare. G. M. Lyon, Huntington.—p. 365.
Medical Service. D. A. MacGregor, Wheeling.—p. 373.
Acute Surgical Abdomen. M. A. Slocum, Pittsburgh.—p. 376.
Back Injuries. H. E. Mock, Chicago.—p. 383.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Physical Medicine, London

8: 69-84 (Sept.) 1933

Ultrashort Electric Waves: New Development in Diathermy. E. Schliephake.—p. 69.
Present Status of Physical Therapy in the United States. R. Kovacs. —p. 72.
Absorption of Infra-Red Radiation by Human Body. B. D. H. Watters. —p. 74.
The Field of the Light Department in a General Hospital. A. E. Rayner.—p. 76.
Practical Dietetics. J. N. Leitch.—p. 77.

British Journal of Urology, London

5: 213-322 (Sept.) 1933

*Pharmacologic Basis of Drug Treatment of Spasm of Ureter or Bladder and of Ureteral Stone. K. Samaan.—p. 213.
*Studies of Urinary Acidifiers and Antiseptics in Relation to Pyelitis and Cystitis. D. R. Mitchell and J. M. Scott.—p. 225.
Carcinoma of the Penis in Siam. T. P. Noble.—p. 242.
Spread of Infection from the Uterine Cervix to the Urinary Tract and Ascent of Infection from Lower Urinary Tract to Kidneys. H. P. Winsbury-White.—p. 249.

Drug Treatment of Spasm of Ureter.—Samaan carried out a series of experiments to determine the degree of action of definite dilutions of papaverine, visammin or atropine on the intestine and the virgin uterus of the rabbit, the ureter of the bull, the human ureter and the bladder of the dog. He found that atropine relaxes the intestine and the virgin uterus of the rabbit, the ureter of the bull and of man and the bladder of the dog if already put in a state of spasm through parasympathetic stimulation, whereas it fails to relax these organs if the cause of the spasm is directly muscular. For the bladder or for the uterus, visammin and papaverine are practically of equal values in relaxing these organs. Relaxation results if the spasm is mediated through the nerve, the muscle or both. Papaverine and visammin relax plain muscle tissue by direct action. In the same concentrations, papaverine is a more efficient drug than visammin on the intestine, while the contrary is true for the ureter of the bull and of man. This makes visammin a drug superior to papaverine in the treatment of spasm of the ureter and of ureteral stone. Relaxation results if the spasm is mediated through the nerve, the muscle or both. The superiority of visammin over papaverine or atropine in relaxing the human ureter as established by pharmacologic experiments led to its clinical trial in cases of ureteral stone. Stones were passed through the natural passages after treatment with a warmed mixture containing 5 cc. of tincture of ammi visnaga (1:10 solution of 90 per cent alcohol) and 30 cc. of decoction of ammi visnaga (1:40) taken three or four times daily with an occasional intermission of the drug.

Urinary Acidifiers and Antiseptics in Pyelitis and Cystitis.—Mitchell and Scott present a clinical study of seventy-five cases of pyelitis and cystitis in which urinary antiseptics and acidifiers were used. They observed that ammonium phosphate and benzoate are effective urinary acidifiers, but a change of p_H has no influence on the infection. Hexylresorcinol, pyridium and helmitol have given no evidence of a urinary antiseptic value. Methenamine in well acidified urine cures at least one third of the nonsurgical cases of pyelitis and cystitis. Methenamine is liberated at the kidney pelvis, at least, and is as effective for pyelitis as it is for cystitis. Resistance to formaldehyde may be due to an individual characteristic of the organism. Focal infection (colonic absorption) seems to have a place in the etiology and treatment of persisting infections of the urinary tract. Urinary infection in simple pyelitis of pregnancy persists and disappears only post partum.

Journal of State Medicine, London

41: 497-558 (Sept.) 1933

Industrial Welfare Under Existing Conditions. T. Oliver.—p. 497.
Economic Test of the Limits of Public Health. J. Stamp.—p. 505.
Airs, Waters and Places: Study of Their Data. G. T. Walker.—p. 511.
Records of Vapor Pressure. F. J. W. Whipple.—p. 523.
Value and Place of Serodiagnosis in the Clinical Investigation of Cancer. E. C. Lowe.—p. 530.
Impressions of the Tuberculosis Problem in Germany. Veronica B. F. Dawkins.—p. 539.
Principles and Practice of Health Education. A. Massey.—p. 545.

Lancet, London

2: 521-572 (Sept. 2) 1933

Experimental Pathologic Studies on Nature and Rôle of Bacterial Allergy. A. R. Rich.—p. 521.
*Generalized Osteitis Fibrosa: Case Successfully Treated by Removal of Parathyroid Tumors. A. L. Abel, G. Thomson and L. M. Hawksley.—p. 525.
Adenoma of Parathyroid Associated with Generalized Osteitis Fibrosa. S. C. Dyke, R. M. Walker and E. Freeman.—p. 530.
Clinical Comparison of Beta and Gamma Ray Therapy for Rodent Ulcer. W. J. O'Donovan and R. T. Brain.—p. 532.
Rectal Incontinence: Causes and Treatment. J. P. Lockhart-Mummery. —p. 535.
Human Trematode Parasite Heterophyes Heterophyes in Egypt: Life History. M. K. Bey.—p. 537.

Osteitis Fibrosa and Parathyroid Tumors.—Abel and his associates report a case of osteitis fibrosa, which was successfully treated by the removal of parathyroid tumors, in a woman aged 58. She had had several attacks of quinsy, acute appendicitis and Bacillus coli pyelitis two years before. Her health was good until the urgent operation for acute appendicitis was performed. After the operation she never felt that she could walk properly. Her strength did not seem to improve, and twelve months before she noticed that instead of becoming stronger she was actually much weaker. She had weakness of all her limbs, but more especially of the right arm. Pain was felt over the middle of the left leg and appeared to be in the bone itself. She always felt tired and faint. The pain in the leg increased, and a swelling appeared over the anterior aspect of the left tibia and increased in size up to 2 inches in vertical diameter. More indefinite aching pains were noticed in the other extremities. Roentgenography showed a cystic area in the left tibia at the junction of the upper and middle thirds and at the inner part of the upper end, involving both the shaft and the epiphysis. The knee joints showed calcification on the surfaces of the cartilages. Microscopic examination showed the changes typical of osteitis fibrosa. Further roentgenographic examination revealed parathyroid tumor. After a rest of ten days and a high calcium diet, the patient was operated on under nitrous oxide-oxygen anesthesia. A Kocher low collar incision was made and the left side was explored first. A superior parathyroid, about three times the normal size, was found and removed. On the right side, four small rounded bodies were found behind the lower part of the thyroid bed. Two were removed for microscopic observation. They were found to be lymph nodes. The thyroid was replaced in its bed, the pretracheal muscles were sutured and the wound was closed, after drainage was provided for. Seventy-two hours after operation the serum calcium had fallen to 12.5 mg. per hundred cubic centimeters. On the sixth day two attacks of paroxysmal tachycardia occurred. Digitalis was administered, with hypodermic injections of morphine. The pulse remained rapid for some days but gradually became normal. A fortnight after operation the serum calcium was still 12.5 mg. Convalescence from then on was quite uneventful. A high calcium diet was administered as soon as possible after operation, with viosterol and ultraviolet radiation. Ten weeks after operation the pains of the bones had disappeared. The patient was steadily gaining weight and was able to walk a little.

Medical Journal of Australia, Sydney

2: 235-264 (Aug. 19) 1933

Further Observations on Chronic Nephritis and Lead Poisoning in Queensland, with Comments on Federal Official Inquiry. L. J. J. Nye. —p. 235.
Treatment of Uterine Cancer. E. T. Thring.—p. 249.
Treatment by Radon of Glandular Extension from Malignant Cervix. L. S. Kidd.—p. 253.

2: 265-298 (Aug. 26) 1933

*Comparison of Blood Sedimentation Rate and Vernes Flocculation Test in Pulmonary Tuberculosis. H. M. James.—p. 265.
Idiopathic Scoliosis. S. H. Scougall.—p. 271.
*Swift's or Pink Disease: Recent Work on Pathology and Treatment. S. F. McDonald.—p. 276.
Investigation into Incidence of Cancerous or Precancerous Skin Lesions Among Tar Workers in New South Wales. Elinor S. Hunt.—p. 281.

Blood Sedimentation Rate and Vernes Flocculation Test in Tuberculosis.—James confirms the work of previous authors in that both the determination of the rate of blood sedimentation and the Vernes flocculation test are of considerable value in the control of the treatment and prognosis in

cases of pulmonary tuberculosis. Provided all precautions were taken, and with certain recognized exceptions, the figures for the two tests were comparable, particularly in infections that were comparatively early or but moderately advanced. In the advanced cases it was felt that the Vernes test represented the clinical condition less accurately than did the rate of blood sedimentation. Of the two methods of investigation, it must be considered that the estimation of the rate of blood sedimentation is more applicable to everyday clinical work and that there is no information given by the Vernes test which cannot equally be supplied by the rate of blood sedimentation. The advantages of the latter method may be summarized as follows: 1. The Vernes test, because of elaborate laboratory methods and material, is a much more expensive test than the sedimentation test. 2. Any medical practitioner can do a sedimentation test at the bedside if necessary. 3. The rate of sedimentation actually gives considerably more information than the Vernes test. In the Vernes test, one has only an end figure. 4. The 1 cc. technic for the sedimentation test is a simple matter for the patient and occasions practically no discomfort. For the Vernes test it is necessary to withdraw at least 10 cc. of blood. For the Vernes test also a fast of about fifteen hours is necessary before the test is made. 5. Blood for the Vernes test must be sent to a laboratory in which there are the requisite facilities. The sedimentation test may be performed anywhere.

Swift's or Pink Disease.—McDonald gives an account of recent work on the etiology and pathology of pink disease. He describes six cases that were apparently benefited by liver treatment. He used a preparation of pig liver. It can be made up as a soup or mixed with other food. Adults generally do not consider it palatable; children with pink disease will often take it freely undiluted. The dose for an adult patient with pernicious anemia is from 5 to 10 cc. three times daily. For the child with pink disease, 5 cc. twice a day is sufficient.

South African Medical Journal, Cape Town

7: 561-602 (Sept. 9) 1933

Combined Anesthesia in Surgery. F. D. du T. van Zyl.—p. 579.

Japanese Journal of Experimental Medicine, Tokyo

11: 253-396 (Aug. 20) 1933

*Anemia Causing Action of Various Hydrazine Derivatives, Their Influence on Oxygen in the Blood and Their Relation to Their Chemical Structure: I. Anemia Causing Action of Various Hydrazine Derivatives and Their Relation to Their Chemical Structure. S. Minami.—p. 253.

Progress of Hemolysis and Some Other Phenomena Relative to Hemolysin. H. Moriyama.—p. 301.

Relation Between Endocrine Gland and Estrus Cycle: Appendix to the First Report: Ovulation in Case of Transplantation of Anterior Lobe of Pituitary Body in the Very Young Female White Rat. S. Tsuchimoto.—p. 349.

*Effect of Bismuth on Experimental Akiyami. T. Moriguchi.—p. 353.

Studies on Variation of Bacterium Dysenteriae (Shigae). S. Takata.—p. 357.

Purification of Vaccinia Virus: Note. H. Yaoi and H. Kasai.—p. 383.

Sterilizing Action of Unsaturated Monobasic Fatty Acids on Putrefactive Bacteria, Bacteria Typhosus and Vibrio Cholerae. S. Tetsumoto.—p. 387.

Anemia-Causing Action of Hydrazine Derivatives.—Minami found no anemia-causing action in hydrazine sulphate. Chemicals that have the benzine nucleus, such as phenylhydrazine, *p*-tolylhydrazine, *o*-metaxylylhydrazine, *p*-nitrophenylhydrazine, *p*-methoxyphenylhydrazine and *p*-ethoxyphenylhydrazine hydrochloric acid, have a fairly strong anemia-causing action. Chemicals having the naphthaline nucleus have also a fairly strong anemia-causing action but show generally slightly weaker action than chemicals having the benzine nucleus. Chemicals having the quinoline nucleus have a weaker anemia-causing action than those having the benzine nucleus. Among the chemicals having the benzine nucleus, if phenylhydrazine hydrochloric acid is taken as the standard and one methyl radical is added to the benzine nucleus of phenylhydrazine hydrochloric acid, the anemia-causing action of the chemical decreases. The action appears to decrease with the increases in the number of methyl radicals. The addition of the nitro radical to the benzine nucleus of phenylhydrazine hydrochloric acid increases the strength of the anemia-causing action. The phenylhydrazine hydrochloric acid having the methoxy radical slightly increases the anemia-causing action and that having the ethoxy radical shows nearly the same degree of anemia-causing action as phenylhydrazine. In the case of the carboxyl radical to the benzine nucleus, the anemia-causing action disappears entirely. The *β*-naphtylhydrazine hydrochloric acid shows a stronger anemia-causing action than the *α*-naphtylhydrazine hydrochloric acid. Anaquinolinhydrazine hydrochloric acid shows a stronger anemia-causing action than orthoquinolinhydrazine hydrochloric acid.

Effect of Bismuth on Experimental Nanukayami.—Moriguchi tested the effect of bismuth on nanukayami (an endemic infectious disease resembling Weil's disease) by infecting guinea-pigs with Spirochaeta akiyami A; the results were satisfactory. After inoculating guinea-pigs with Spirochaeta akiyami A, he injected subcutaneously a 1 per cent solution of potassium and sodium bismuth tartrate every twenty-four hours, using 1 cc. per hundred grams of the body weight. The controls showed characteristic symptoms of nanukayami and had spirochetes in the liver. No animal injected immediately after inoculation developed symptoms of nanukayami. As no spirochetes were noted by dark field examination, the author made an emulsion of the liver to verify whether or not it had infective power for test animals and found that it had not. Seven animals were injected twenty-four hours after inoculation, of which two were observed to live normally for more than a month. The others died, but no lesion was discovered at necropsy to implicate nanukayami as the cause of death. Of three animals injected forty-eight hours after inoculation, one lived more than a month, and the other two showed no lesions of nanukayami at necropsy. The animals injected seventy-two hours after inoculation followed the same fate as the controls in one or two days. But the symptoms peculiar to nanukayami were much slighter and no spirochetes were discovered in the liver. The author shows that potassium and sodium bismuth tartrate has a positive effect when injected within forty-eight hours after inoculation (and even when injected seventy-two hours after inoculation) and concludes that potassium and sodium bismuth tartrate has a remarkable effect both as a preventive and as a curative.

Journal of Oriental Medicine, South Manchuria

10: 13-22 (Aug.) 1933

Observations on Recent Mortality Statistics of Japanese in Manchuria: Part I. S. Kawahita.—p. 13.

Id.: Part II. S. Kawahita.—p. 16.

Effect of Sulphur on Antitoxic Function Against Hydrocyanic Acid. C. Tsuru.—p. 18.

Comparative Study of Various Solid Cultural Mediums and Kirchner's Fluid Medium: Isolation of Tubercle Bacilli. H. Hiroki and K. Urabe.—p. 19.

Effect of Various Metal Salts on Therapeutic Action of Arsphenamines in Spirochetosis. H. Hiroki.—p. 20.

Effect of Reflexes Produced by Stimulation of Second and Third Trigeminal Branches on Respiration and Blood Pressure. G. Nakamura.—p. 21.

10: 23-38 (Sept.) 1933

Experimental Investigations on Persistence of Spironema Recurrentis in Brain. H. Hiroki.—p. 23.

Biochemical Studies on Nitril: Part I. (Supplement No. 2). Formation of Rhodan Compound Within the Bodies of Lower Vertebrates. C. Tsuru.—p. 27.

Effect of "Pechka" Heating on Ventilation. K. Matsuoka.—p. 28.

Clinical Stand Against Assumption of Respiratory Paralysis as Cause of Death in Spinal Anesthesia with Tropacocaine. K. Shimatsuma, T. Imagawa and H. K. Su.—p. 29.

***Slowly Developing Meningococcus Sepsis"? and Its Treatment with Trypaflavine. K. Kashiwahara.—p. 30.

Rhodan Compound Content of Serums of Various Animals. C. Tsuru.—p. 31.

Pathologic Histology of Sclerosis of Lymph Nodes. E. Kitahatake.—p. 33.

Experimental Studies of Postdiphtheritic Paralysis: Chapter IV. Histologic Studies on Central Nervous System in Case of Postdiphtheritic Paralysis. T. Maki.—p. 34.

Patterns of Ridges of Skin on Toes of Chinese. S. Takeya.—p. 36.

Treatment of Meningococcus Sepsis with Acriflavine Hydrochloride.—During the last few years, Kashiwahara encountered five cases which presented high remittent fever, eruptions closely resembling erythema nodosum and arthralgia. He made clinical observations in each case and states that the present cases most closely corresponded in their clinical appearance with the "slowly developing meningococcus sepsis" described by Friedmann and Deicher. However, he could not demonstrate meningococci in the blood of each patient. He used injections of acriflavine hydrochloride and cured each patient.

Journal de Chirurgie, Paris

42: 497-672 (Oct.) 1933

Technical Point in Resection of Cancerous Breast. P. Duval and H. Redon.—p. 497.
Surgery of Parathyroids. H. Welti and A. Jung.—p. 501.
*Immediate Treatment of Fractures of Base of Skull. C. Lenormant, P. Wertheimer and J. Patel.—p. 529.
Surgical Treatment of Severe Gastroduodenal Hemorrhages of Ulcerous Origin. F. Papin and P. Wilmoth.—p. 539.

Immediate Treatment of Fractures of Base of Skull.—Lenormant and his associates say that, in the first twenty-four hours, abstention from treatment is indicated on the one hand in hyperacute cases exhibiting signs of prostration, fever of 40 C. (104 F.) and abolition of the corneal reflex and, on the other hand, in so-called benign cases in which the symptoms recede quickly. Signs of intracranial hematoma are an indication for surgical treatment. If an extradural hemorrhage is discovered after the skull has been opened, the clots must be carefully removed and the source of the hemorrhage located if possible. If temporal trepanation discloses a dura mater that is violet and taut and the clinical signs indicate intracranial hematoma, the meninges should be incised. If neither an extradural nor a subdural hematoma is found, exploration of the opposite side of the head may disclose a countercoup lesion. In cases of deep intracranial hematoma, the results of this second examination are negative. In the cases of grave cerebral concussion the choice of treatment is governed by the succession of physiopathologic phenomena. It is of prime importance to measure the arterial and spinal fluid pressure, as the symptoms of hypotension and hypertension are often similar. In primary hypotension, from 20 to 40 cc. of distilled water should be injected intravenously and, if this fails, from 500 to 1,000 cc. of physiologic solution of sodium chloride. In hypertension there is the choice between lumbar puncture with manometric control and hypertonic medication. In certain grave cases, interpretation of the signs is uncertain although indispensable to rational treatment. The cause of a syndrome of intracranial hypertension may remain obscure and the Queckenstedt-Stookey test and measurement of the tension of the central artery of the retina may be necessary to determine whether the hypertension is free or blocked. In the latter case, ventricular exploration by puncture at the inferior occipital point may disclose one of three conditions. Both ventricles may be obliterated by cerebral edema or, rarely, bilateral hematomas: bilateral temporal trepanation is the only logical therapy under those circumstances. If one of the ventricles is dilated while the other one is obliterated, trepanation of the fornix on the affected side is indicated. If the result is negative, evacuation of the dilated ventricle by puncture is indicated. In some cases, ventricular puncture may disclose dilatation of both ventricles. This may be due to obliteration of the passages connecting the intracerebral system with the subarachnoid spaces or to the insufficiency of these passages. Withdrawal of ventricular fluid may suffice if the drainage passages are free; if they are not, repeated evacuations will bring no improvement and drainage of the subarachnoid spaces at the posterior cisterna magna is required. The authors discuss the treatment to be given after the first thirty-six hours in cases that did not show early improvement. Continued hypotension demands the injection of water or physiologic solution of sodium chloride. Secondary hypertension is much more frequent. It imposes temporal trepanation in cases in which a reassuring clinical picture in the first twenty-four or forty-eight hours is succeeded by more complete coma, epileptiform crises or paralyses, indicating a localized lesion. Temporal trepanation is not satisfactory in exacerbation of the concussion syndrome with discovery of blood in the subarachnoid spaces indicating compression or irritation of the medulla and in cases in which cerebrospinal block exists. In the latter cases if the fluid obtained by suboccipital puncture is bloody and hypertensive, the block is perimedullary or cervical; if it is not, the obstacle is located higher up. In cases of hypertrophic concussion, trepanation with an osteoplastic flap (Arnaud) on both lateral surfaces of the fornix or, perhaps, posterior trepanation may be employed, but in all other cases suboccipital drainage is indicated.

Presse Médicale, Paris

41: 1681-1704 (Nov. 1) 1933

Migratory Projectiles. R. Prédelièvre and P. Étienne-Martin.—p. 1681.
*Combination of Vaccine Therapy and Serum Therapy in Preventive Treatment of Tetanus. Mme. C. Clavel and C. Clavel.—p. 1683.
*Specificity of Weinberg Reaction in Diagnosis of Echinococcosis. J. Outeirino Nunez and M. Calvelo Lopez.—p. 1684.

Vaccine and Serum Therapy in Prevention of Tetanus.—The Clavels state that in rare instances patients have succumbed to tetanus or presented manifestations of attenuated tetanus despite correctly executed surgical disinfection and prophylactic serotherapy. To prevent such occurrences they recommend that antitetanus serotherapy be supplemented by vaccination with tetanus anatoxin in cases in which the patient has one or more wounds that may remain infected with tetanus bacilli for a long time. To the passive immunity, rapidly induced by the serotherapy but of brief duration, vaccination adds an active immunity, which is slowly produced but of very long duration. The combined therapy gives the patient a maximal guarantee against the danger of tetanus which is not only an immediate but a long term menace in certain cases. Vaccination with anatoxin is absolutely innocuous; it may be employed simultaneously with serotherapy and confers an immunity that lasts for several years. Vaccination with anatoxin is indicated in the case of a wound the evolution of which is long and may require successive interventions. Conservative interventions require antitetanic vaccination more than amputations, as they often take longer to heal and may retain a tetanus infection despite the vigilance of the surgeon. Vaccination is also indicated in case of multiple traumas, since in the presence of a grave trauma, as for instance rupture of the spleen, smaller wounds of the face or the extremities might receive insufficient attention. In the aforementioned cases the authors give an injection of from 10 to 20 cc. of antitetanus serum immediately after the accident. Then with another syringe and at a different point, a subcutaneous injection of 0.5 cc. of anatoxin is given; ten days later they inject 1 cc. of anatoxin and two months later 2 cc. of anatoxin. In case of reintervention several months or years later, from 1 to 2 cc. of anatoxin is again injected, and in this case a new antiserum injection can probably be dispensed with. In time of war all soldiers should receive antitetanus vaccination and in civilian practice it should be given to all laborers whose profession exposes them to frequent injuries susceptible to tetanic infection.

The Weinberg Reaction in Diagnosis of Echinococcosis.—From a series of experiments, Outeirino Nunez and Calvelo Lopez conclude that the Weinberg reaction, a complement fixation reaction for the diagnosis of echinococcosis which uses the fluid from hydatid cysts of sheep as antigen, is not specific for hydatid disease but is rather a group reaction. This conclusion is based on the following experimental results: 1. The antigen prepared by them from Taenia saginata (alcoholic extract) fixes complement in the presence of serums of patients with hydatid cysts with intensity as great as or greater than the fluid from the cysts of sheep. 2. The serums of patients harboring intestinal taenias, of animals infested with various forms of taenia or their embryos, and of animals immunized by parenteral administration of proteins derived from these parasites give equally positive reactions with the extract of taenia and with the hydatid antigen. 3. Positive results were also obtained with both antigens in certain nonparasitic diseases. 4. In general, inactivation is followed by the destruction of amboceptors in varying degrees, the reactions being weaker with the heated serums than with those used without inactivation.

Schweizerische medizinische Wochenschrift, Basel

63: 1121-1144 (Nov. 4) 1933

Appendicitis: Cases Observed from 1928 to 1932 at Hospital Frauenfeld. W. Ider.—p. 1121.
*Tissue Injuries of Chemical Origin, Particularly Necroses Caused by Ink Pencils. J. de Puoz.—p. 1124.
*Icterus Neonatorum Gravis with Especial Consideration of Infectious Type. H. Fuchs.—p. 1129.
Determination of Blood Sedimentation. W. Hadorn.—p. 1134.
Pemphigus: Case. G. Franck.—p. 1138.

Injuries Caused by Ink Pencils.—Experimental and clinical observations convinced de Puoz that the noxious agent in

ink pencil injuries is the dyestuff component, which is always an aniline dye. The greater the alkalescence of the dyes, the greater also their harmfulness. A prolonged influence of the aniline dyes results in headaches, loss of appetite, general debility and increased temperature. Early appropriate treatment prevents the general reactions. Studies of the local symptoms disclosed that the portions of the ink pencil that have entered the tissues are dissolved by the tissue fluids. The dissolved dye becomes diffused and exerts a necrotizing effect. The injuries produced by ink pencils are particularly severe when they involve a mucous membrane, especially the conjunctiva, where they produce extensive ulcerations. The author gives a summary report of thirty-three injuries produced by ink pencils. This report indicates that surgical therapy gives better results than conservative measures. The author recommends the radical excision of all tissues that have become discolored by the dye. Subsequent irrigation with tannin and wet dressings accelerate the healing process, and some authors have seen favorable effects from after-treatment with ultraviolet rays.

Icterus Neonatorum Gravis.—In a review of the literature on icterus neonatorum gravis, Fuchs shows that it largely concerns itself with the familial form. It is his aim, however, to differentiate distinct groups and to call particular attention to an infectious form. In four children, who developed a severe icterus during the first three days of life, he discovered a septic infectious process either during life or in the course of the necropsy. In three of them the infection originated in the umbilicus. All four children had convulsions or spasm of the muscles of the extremities as signs of a cerebral involvement. The children were apathetic and did not nurse normally. Their stools showed biliary discoloration. The blood either showed no erythroblastosis or the values were still within normal limits. In three cases the urine contained dissolved bilirubin. All but one of the children died within the first two weeks of life. Since the children were the first ones in their families to develop icterus neonatorum, the cases could not be definitely diagnosed as the familial form. The first two of the children were siblings, and consequently the familial form could be thought of; since the most characteristic symptom, erythroblastosis, was absent, however, the diagnosis was not made. The author considers it probable that this family may have a predisposition to severe icterus or a susceptibility to infections. In the second and third cases the same bacterial flora was found in the vagina of the mother and in the umbilical pus of the infants. The fourth infant showed nearly all the signs of the familial form of icterus neonatorum gravis. The presence of the septic infection was the only factor that militated for a differential diagnosis of infectious icterus neonatorum. In his discussion of the familial form, the author shows the significance of the differentiation between the two forms. In addition to these two types he recognizes yet a third type of icterus neonatorum gravis. To this group he assigns all cases that are neither familial nor infectious. Whether in this third form there exists a deficient capacity for independent extra-uterine existence cannot be definitely determined as yet.

Archivio Italiano di Chirurgia, Bologna

34: 749-864 (Sept.) 1933

*Pulmonary and Thoracic Actinomycosis. P. Foltz and G. Canavero. —p. 749.
Experiences in Numerical Enrichment and Method of Distribution of Fibers in Nerve Regeneration. A. M. Dogliotti.—p. 781.
*New Method of Approach to First Two Ribs in Operation of Apicolysis. R. Broglio.—p. 819.
Frei Test in Inguinal Lymphogranulomatosis. M. Cattaneo.—p. 829.
Variations of Calcium Content of Blood Serum in Animals Operated on for Sympathectomy of Superior Thyroid Arteries. A. Previtera. —p. 846.

Pulmonary and Thoracic Actinomycosis.—Foltz and Canavero made a study of a patient suffering from bilateral pulmonary actinomycosis with involvement of the pleura and the thoracic wall. The authors do not recognize the existence of two separate forms of pulmonary actinomycosis, the superficial and the ulcerative. They demonstrate that it has no anatomic basis but only a pathogenic one. They distinguish between actinomycosis involving pulmonary tissue alone (superficial actinomycosis of other authors) and that of a pulmonary thoracic variety. In the latter they distinguish between pulmonary actinomycosis spreading to the thorax and primary actinomycosis of the thorax spreading to the lung. Regarding the pulmonary origin of the pulmonary thoracic form, the authors attribute the notable presence of pseudo-adenomatous formations to proliferation of the bronchial epithelium.

Approach to Ribs in Apicolysis.—Broglio describes the following operative technic: The patient assumes the position ordinarily used in intervention on the thyroid with the head extended and turned slightly away from the side operated on. The intercostal nerves are blocked with a 0.5 per cent solution of tutocain, and a 0.25 per cent solution is used for infiltration anesthesia. A rectangular incision is made, starting 5 cm. above the sternoclavicular articulation, passing over the joint and ending at the upper margin of the second costal cartilage; the horizontal limb of the incision follows the upper margin of the second rib and stops at the outer third of the clavicle. About 40 cc. of the anesthetic is used for further infiltration. The aponeurosis of the supraclavicular fossa is divided, the sternoclavicular articulation is opened and the muscular bundles of the pectoralis major are divided 1 cm. from their insertion on the sternum together with the aponeurosis. Blunt dissection separates these bundles from the rest of the pectoralis muscle and stops at the vascular pedicle. The posterior aspect of the sternoclavicular articulation is separated from the surrounding tissues and the clavicle is dislodged and freed. The upper aspect of the first and second ribs is anesthetized and the periosteum is detached, care being taken to avoid division of the pleura. The ribs are resected at their union with the costal cartilage and at a point beyond the posterior costal angle. The operation is completed by replacing the luxated extremity of the clavicle and reconstructing the planes of the thoracic wall. The clavicle is held in place by fibroperiosteal sutures made with interrupted catgut. A rubber tube is placed at the external angle of the wound to assure drainage and is removed in clean cases after forty-eight hours. The great advantage of this method is the possibility of resecting the ribs under visual control.

Medicina Ibera, Madrid

2: 533-564 (Oct. 21) 1933

Effects of Liver and Stomach Preparation on Experimental Anemia. C. Elósegui and F. Llopis.—p. 533.
*Intravenous Alcohol Injections in Treatment of Pneumonia. E. Jaso and M. Quero Malo.—p. 542.
Surgical Therapy in Tumors of Renal Pelvis. S. Pascual.—p. 553.

Alcohol Injections in Pneumonia in Children.—Jaso and Quero Malo advise the use of intravenous injections of alcohol in the treatment of pneumonia in children. The injections consist of 5 cc. of a 33 per cent solution of alcohol in physiologic solution of sodium chloride, preferably given as soon as the diagnosis is made and repeated daily until the crisis of the disease is reached. It is advisable to increase the dose in children more than 6 years of age. The injections have an antithermic effect and also a regulating effect on the pulse. The temperature shows a tendency to become normal following the first injection. The treatment has no influence on the rate of respiration. It has, however, a favorable influence on the disease by maintaining the resistance of the patients so that they go through the disease in a good general condition, do not lose their appetite and do not have diarrhea as a complication. It has also a favorable influence on the evolution of the pulmonary condition, which is manifest by the early appearance of crepitant râles on the third or fourth day of the disease and by the rapid resolution of the pulmonary lesions and disappearance of the pulmonary infiltration, as proved by roentgen examination of the lungs. The duration of the pneumonia is greatly decreased, especially when the injections are given from the first day of the disease. In these cases the disease follows a benign evolution and its duration is of not more than five days. The percentage of mortality from pneumonia in children is greatly reduced by the administration of this treatment. The author has obtained satisfactory results in fifteen cases, of which twelve were lobar pneumonia and three bronchopneumonia.

Deutsche medizinische Wochenschrift, Leipzig

59: 1639-1688 (Nov. 3) 1933

*Pneumoroentgenography of Knee Joint and Its Practical Results. H. Schum.—p. 1639.
Psychiatric Treatment. K. Schneider.—p. 1663.
*Relations Between Clinical Aspects of Lead Poisoning and Lead Content of Blood and Urine. E. Bass.—p. 1665.
Transmutability of Bacteria with Especial Consideration of Bacterium Typhi-Flavum. G. Schernheim.—p. 1668.
Climatotherapy During Fall and Winter. F. Linke.—p. 1669.
After-Treatment in Spas. H. Determann.—p. 1670.
Thoughts at Conclusion of Treatment in Spas. P. Schober.—p. 1672.
After Treatment? R. von den Velden.—p. 1674.

Pneumoroentgenography of Knee Joint.—Schum maintains that internal injuries of the knee joint cannot be detected by means of the ordinary clinical examination. In order to avoid unnecessary arthrotomies and yet be able to make a definite diagnosis, he employs pneumoroentgenography. The needle, which he employs for the introduction of air into the joint, resembles the pneumothorax needle; that is, it is closed at the end and has the opening at the side. This arrangement prevents undesirable air inflation of the tissues. The lumen of the needle should not be too narrow, so that articular exudate which may be present can be discharged through it. The discharge of such an exudate indicates that the needle is located properly in the articular cavity, and the complete elimination of this fluid is an absolute requirement for the success of the roentgenography, since otherwise the air cannot penetrate into the different spaces. The inflation of the joint is done slowly. Since complete expansion of the capsule is absolutely necessary, 60 cc. of air is the least that should be introduced, but in some cases as high as 200 cc. can be injected. However, excessive amounts are not advisable, because emphysema of the soft parts will cause a distortion of the roentgen picture. All roentgenograms are made stereoscopically. One exposure is made in the sagittal plane and the other vertically to it. Occasionally an oblique exposure may be helpful. Since the demonstration of changes in the ligaments, cartilages and menisci is the primary object of pneumoroentgenography, the author employs soft ray tubes and makes the exposures as short as possible. He used this method in 233 examinations on 190 patients and never observed complications. He discusses the pathologic conditions that he discovered in the course of these examinations, such as joint mice, injuries of the crucial ligaments and of the menisci, ruptures of the cartilages and deformities of the capsule. He calls attention to the fact that air inflation of the knee joint can be used also for therapeutic purposes. He states that patients with chronic dropsy frequently asked for a new air filling because it gave them great relief. He found it helpful also in postoperative exudates and in exudates caused by injuries. In case of posttraumatic accumulation of blood or fluid, a single injection of air may be sufficient, and even inflammatory exudates, which rarely yield to puncture alone, have yielded to air filling.

Lead in Blood and Urine of Patients with Lead Poisoning.—Bass points out that the diagnosis of lead poisoning may be difficult in cases in which the lead line, stippled erythrocytes and porphyrinuria are absent. Until recently the methods for the quantitative determination of the lead content of blood and urine were inadequate. However, since P. Schmidt and his co-workers devised an electrolytic-colorimetric method, the analysis of blood and urine has proved helpful in the diagnosis, in the evaluation of benefit claims and in the estimation of the efficacy of therapeutic procedures. The method developed by Schmidt extracts the lead by precipitating the incinerated material with hydrogen sulphide, and by electrolysis the lead is deposited at the anode in the form of lead superoxide. By immersing the latter in a solution of tetramethyldiaminodiphenylmethane in glacial acetic acid a blue dyestuff is obtained and is then colorimetrically compared with a comparative solution. The margin of error never exceeds 0.02 mg. Thus the procedure has a sensitivity that permits the detection of the smallest quantities of lead. The author notes that entirely healthy persons, who have never come in contact with lead, have minute amounts of lead in their blood and urine, the average being 0.02 mg. in 100 cc. of blood or in 1,000 cc. of urine, respectively. As the threshold values above which signs of lead poisoning tend to appear, Schmidt and his co-workers have given a lead content of 0.06 mg. in 100 cc. of blood and of 0.1 mg. in 1,000 cc. of urine. From observations on forty patients with lead poisoning, the author concludes that the quantitative determination of the lead content of the blood and urine is of great value in the diagnosis and estimation of lead poisoning, but careful clinical observation cannot be dispensed with.

Deutsches Archiv für klinische Medizin, Berlin

173: 637-700 (Oct. 25) 1933

Diagnosis of Syphilis of Joints. Z. Gerškovič and M. Brenner.—p. 637.
*Osteoporotic Obesity (Pituitary Basophilism). E. Rutishauser.—p. 640.
Criticism of Alkaline and Acid Methods for Determination of Iodine Content of Blood. H. Lücker.—p. 681.
Diagnosis of Disturbances in Pancreatic Ferments: Diastase Content of Blood in Diseases of Biliary Passages and of Duodenum. J. Brinck and Rodriquez-Olleros.—p. 691.

Osteoporotic Obesity (Pituitary Basophilism).—Rutishauser emphasizes that osteoporotic obesity must be differentiated from adiposogenital dystrophy (Fröhlich's syndrome), with which it has two symptoms in common; namely, obesity and hypoplasia of the genital organs. The differentiation can be based on the presence of osteoporosis and of high blood pressure and on the absence of visual impairment and of increased cerebral pressure, the latter two symptoms being nearly always present in adiposogenital dystrophy. The hypophyseal, changes which the author observed in osteoporotic obesity are the following: a small basophil adenoma of the anterior lobe; numerous nodule-like, basophil hypertrophies and severe malformations in the region of the posterior lobe, the latter being interpreted as an agenesia, and increase in the basophil cells involving the entire anterior lobe. In one case an alcoholic cirrhosis of the liver existed. The increase in the basophil cells does not necessarily have to assume the form of an adenoma. In two cases, in which a basophil adenoma of the hypophysis could not be found, the increase in basophil cells could be traced to the primary disease, in the second case to agenesia of the posterior lobe of the hypophysis, and in a third case to alcoholic cirrhosis of the liver. The author found that the suprarenals were either well developed or hypertrophic. The hypertrophy involved both the cortex and the medulla. The ovaries were atrophied. In one case it never came to the development of the graafian follicles. The thyroids were atrophic, were poorly developed or showed degeneration of the colloid or goiter. The parathyroids were lipomatous but not always equally severe in all four parathyroids. The changes in the skeleton were of an osteoporotic nature, and in two cases the osteoporosis caused spontaneous fractures of the ribs.

Münchener medizinische Wochenschrift, Munich

80: 1729-1764 (Nov. 3) 1933

Recent Observations on Venous and Pulmonary Circulation. M. Hochrein.—p. 1729.
Diagnosis and Treatment of Ulcers of Stomach and of Duodenum. H. Schlecht.—p. 1734.
*Hypertension and Acidity of Tissues. W. Scharpff.—p. 1739.
*Fever Therapy of Trigeminal Neuralgia. T. Böckheler.—p. 1740.
Ergot Against Gangrene. W. Gerlach.—p. 1743.
Rejection of General Use of Thorium Dioxide Preparation as Contrast Medium in Pyelography. O. Hennig and J. Lechnir.—p. 1746.
Nervous Disturbances and Invalidism. A. Hanse.—p. 1747.
Case of Dropsy in Eighteenth Century: Contribution to History of Diagnosis of Cardiac Disturbances. L. Norpoth.—p. 1749.
Circulation and Respiration in Pulmonary Tuberculosis and Its Significance in Deciding Collapse Therapy. R. Cobet.—p. 1753.

Hypertension and Acidity of Tissues.—Scharpff calls attention to studies which revealed that an abnormal retention of alkali is demonstrable in disorders with a vasoneurotic component (gastric ulcer, asthma, hypertension). Investigators who studied this problem in patients suffering from hypertension found that the retention of alkali is greater in younger persons than in older ones. To verify this observation the author decided to study alkali retention in older patients having hypertension. The average age of the forty patients, whom he subjected to a sodium bicarbonate tolerance test, was 58 years. Following elimination of the morning urine, the patients rested another hour and then evacuated the bladder once more,

or a specimen was withdrawn with the catheter (test urine 1). Then they were given an intravenous injection of 20 cc. of a 10 per cent solution of sodium bicarbonate, and two hours later the bladder was emptied once more (test urine 2). The degree of acidity of the two specimens was determined by means of the colorimetric method of Wulff. The results were not uniform. The differences in the p_H values of the two specimens fluctuated between 0.3 and 2.0, and in one case the p_H value was not changed at all. If the difference in the two specimens is slight, the alkali has been retained in the tissues of the patient; if it is great, the elimination is good. The author observed that the treatment effected a considerable reduction in the blood pressure of patients who eliminated the alkali well, whereas the therapy was ineffective in those who retained large portions of the alkali. Thus the test is an aid in forecasting the probable development of hypertension.

Fever Therapy of Trigeminal Neuralgia.—In the treatment of trigeminal neuralgia, Böckheler employed a preparation which contains proteins from nonpathogenic bacilli, primarily of the colon group. The first injection was generally made with 50 units, the second with 100, the third with 200 and so on until 500 units is reached. The total number of injections is usually from five to six, but in some cases from three to four may be sufficient, and in refractory cases from seven to eight injections may be given. The fever begins usually from one to two hours after the injection. During the following two or three hours it increases to from 39 to 40 C. (102.2 to 104 F.) and after another six or eight hours it begins to decline again. In the cases of trigeminal neuralgia, but also in other forms of neuritis, it was found that the greater the pain reaction of the involved nerve during the fever the better was the therapeutic result. Complications or injurious effects were never observed. The author gives the case reports of a number of patients who were subjected to this form of fever therapy. He does not wish to create the impression that fever therapy should replace surgical therapy entirely, but he thinks that, if his results with fever therapy could be duplicated by others, it would be advisable to try fever treatment first, and to employ surgical treatment only as a last resort.

Zeitschrift f. d. ges. Experimentelle Medizin, Berlin

91: 1-266 (Oct. 21) 1933

Experimental Investigations on Spastic or Peptic Genesis of Acute Hematogenic Pilocarpine Gastritis. H. Hanke.—p. 1.
Experimental Investigations on Production of Necroses by Infection and Simultaneous Modification of Blood Circulation. P. Schmidt-Yeyland.—p. 34.
Fermentative Hemolysis. D. Kanócz.—p. 56.
*Modification of Blood Pressure by Moor Baths. H. Guthmann and L. Hess.—p. 66.
Rôle of Reticulo-Endothelial System in Fibrinogen Formation. A. Lesaler and L. Paulicsky.—p. 86.
Functional Capacities of Pars Intermedia of Human Hypophysis: Investigations on Content and Site of Formation of Melanophoric Hormone. A. Jores and O. Gloger.—p. 91.
Absorption of Iodine from Baths Through Skin and Its Fate in Organism. H. Anthes and F. Salzmann.—p. 100.
Investigations on Action Mechanism of Contra-Insular Hormone of Anterior Lobe of Hypophysis: Anterior Lobe of Hypophysis, Thyroid and Carbohydrate Metabolism. H. Lucke, E. R. Heydemann and F. Duensing.—p. 106.
*Carbon Dioxide Inhalation in Treatment of Bronchial Asthma. P. Faragó.—p. 114.
Experimental Investigations on Problem of "Trypsin Intoxication" in Acute Pancreas Necrosis: Sensitive and Exact Method for Quantitative Determination of Trypsin. J. Baumann.—p. 120.
Edema Tendency and Serum Lipoid Quotient. H. Kürten.—p. 178.
Determination of Length and Position of Digestive Tract: Studies on Dead and Living Dogs for Comparison of Intravital and Postmortal Conditions. R. Nickel.—p. 193.
*Studies on Uric Acid Regarding Hyperuricemia of Renal Origin. W. Voigt.—p. 244.
Influence of Duration of Moistening of Solids on Their Capacity to be Moistened. H. Lampert.—p. 253.
Influence of Sulphide, Sulphite and Sulphate Compounds on Metabolism. M. Kojima.—p. 257.

Modification of Blood Pressure by Moor Baths.—In studies on the influence of moor baths on the blood pressure, Guthmann and Hess found that under the influence of the baths the daily fluctuations in blood pressure are comparatively mild. The less hot moor baths effect a greater reduction in the systolic pressure than do the hot baths. In contradistinction to other investigators, the authors found that after hot baths there was no increase in the systolic pressure over the initial value, either in the average values or in the greatest number of individual cases. To be sure, the number of patients who show a short increase at the beginning and end of the bath increases with the temperature of the bath, but they always remain in the minority. The diastolic pressure decreases immediately after the onset of the bath. In the hotter baths this decrease is somewhat slower. The amplitude is temporarily increased during the bath, and this increase is not merely the result of the further decrease of the diastolic pressure but particularly of the comparatively lesser decrease in the systolic pressure. Hotter baths effect a greater increase in the amplitude; in baths that are less hot the maximal increase in the amplitude takes place during the first part of the bath, while in the hotter baths the maximal amplitude is reached during the second half. The effect of water baths of the same temperature and of the same duration as moor baths is generally less prolonged. The quantitative changes likewise are often lesser. Under certain conditions, half moor baths of higher temperatures produce the same reactions as full moor baths of lower temperatures. By varying the mode of application (full and half baths) and the temperature and the duration of the baths, the reaction can be adjusted to the individual case. A complete series of moor baths does not change the blood pressure within certain limits. The primary blood pressure must be taken into consideration when the type of moor baths is decided. In case of hypotension, the patient has to be watched during the bath, because there is danger of collapse. This applies particularly to the hot baths with their greater action on blood pressure and pulse acceleration.

Carbon Dioxide in Treatment of Bronchial Asthma.—Faragó shows that, in addition to the medicinal and dietary treatments, carbon dioxide inhalation has a certain place in the symptomatic treatment of bronchial asthma. He found that some asthmatic attacks and dyspneas can be favorably influenced by the inhalation of an 8 per cent mixture of carbon dioxide and oxygen. The inhalation of this mixture effects a decrease in the alkali reserve and an increase in the lactic acid content of the blood. The p_H of the urine remains the same, while the ammonia elimination decreases.

Uric Acid and Hyperuricemia of Renal Origin.—Voigt recommends Folin's micromethod for the determination of uric acid. He stresses the advantages of the method, particularly its reliability. In order to illustrate renal insufficiency caused by "endogenic overburdening" with nitrogenous waste matter, especially uric acid, he describes a case in which pneumonia was complicated by nephritis. The renal insufficiency became manifest in the retention of large amounts of nitrogenous waste matters in the blood. The curve indicating the uric acid content of the blood was determined by means of pyrogenic uric acid tolerance tests in normal persons as well as in the patients having renal insufficiency. In normal persons presenting mild fever the curve rises only slightly, and after cessation of the fever the curve immediately returns to the normal level. In patients suffering from renal disturbances, however, the curve indicating the uric acid content rises comparatively high and the decline is extremely retarded. The uric acid content during rest and while the person is fasting shows a surprising individual constancy in normal persons, but in persons having renal insufficiency there are great fluctuations, corresponding to the impaired eliminatory function of the kidney. The difference between the uric acid content of the blood and of the cantharides blister in patients having renal insufficiency makes possible the interpretation of a hyperuricemia and helps in determining its renal origin. In the case in which pneumonia concurred with nephritis, the disappearance of the renal insufficiency was accompanied by a steplike decrease in the difference between the uric acid content of the blood and of the cantharides blister. In latent renal insufficiency an artificial fever of short duration increases the difference between the uric acid content of the blood and of the cantharides blister to an extent that in persons without renal disturbances can be obtained only if the fever is high and prolonged.

SUBJECT INDEX

This is an index to all the reading matter in THE JOURNAL. In the Current Medical Literature Department only the articles which have been abstracted are indexed.

The letters used to explain in which department the matter indexed appears are as follows: "BI," Bureau of Investigation; "E," Editorial; "C," Correspondence; "ME," Medical Economics; "ab," abstract; the star (*) indicates an original article in THE JOURNAL.

This is a subject index and one should, therefore, look for the subject word, with the following exceptions: "Book Notices," "Deaths," "Medicolegal Abstracts" and "Societies" are indexed under these titles at the end of the letters "B," "D," "M," and "S." State board examinations are entered under the general heading State Board Reports, and not under the names of the individual states. Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

For author index see page 2211.

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Acad.—Academy
Am.—American
A.—Association
Coll.—College
Conf.—Conference
Cong.—Congress
Conv.—Convention
Dist.—District
Hosp.—Hospital
Internat.—International
M.—Medical
Med.—Medicine
Nat.—National
Pharm.—Pharmaceutical
Phys.—Physicians
Soc.—Society
Surg.—Surgery
Surgs.—Surgeons

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